Abstract
Tuberculosis (TB) is a major public health concern as around two billion of the global population is latently infected. Mycobacterium tuberculosis (Mtb) is the etiological agent of TB. It is clever enough to escape from the immunological response of the host. It uses specific strategies to maintain its survivability as the pathogenesis of the bacterium is achieved through the molecular interaction between microbial product and the host proteins. This leads to the changes in the host cell mechanism. It not only arrests the steps of maturation of phagosome but also modulates the tissues by releasing potent, bioactive cell wall constituents. Several mycobacterium proteins play crucial role in establishing the infection by interacting with the host proteins and manipulating the host proteins that produce immune response against the pathogen.

This review is focused on the etiology of Mtb, its mechanisms of survival and the importance of the host pathogen interaction analysis in understanding the infection process, as it is an emerging and evolving field that can assist in the development of new therapeutic target.

Keywords: Mycobacterium tuberculosis, tuberculosis, host pathogen interaction, survival strategy, pathogenesis.

Introduction
Tuberculosis (TB) is a devastating disease caused by infectious agent Mycobacterium tuberculosis (Mtb). It is a major international health problem. World Health Organization (WHO) declared TB as a global public health emergency in 1993. The control of TB was impeded because the bacterium started showing resistance towards the first line drug i.e. Isoniazid (INZ) and Rifampicin (RIF)\(^1\). In 2017 the estimated number of TB occurrence was 10.0 million, comprising 3.5 million incidences in women and one million cases in children. Total 1.3 million deaths were caused from TB including 0.4 million deaths from HIV.

In India, there were about 2.8 million incident cases of TB i.e. approx. 28 % of total cases\(^2\). At present, TB is a leading cause of mortality followed by Human Immunodeficiency Virus (HIV), in spite of having powerful tools and techniques for vaccination, diagnosis and treatment of TB\(^3\). Mtb is highly troublesome pathogen because it hijacks the host macrophages and utilises it to replicate within. This is an effective strategy of Mtb for its survival inside the host cell\(^4\).

Pathogen dependent inhibition of the phagosome-lysosome fusion is one of the defence mechanisms of Mtb to survive within the host macrophages\(^5\). It also develops drug resistance through mutations or horizontal gene transfer mediated by phages, plasmids or transposon elements which make them grow in the presence of antibiotics and as a result the chemotherapeutics against TB treatment are severely limited\(^6\).

The development of TB depends on the virulence and pathogenesis of the bacterium. There are several mechanisms involved from the pathogen as well as the host side that play vital role in establishing the disease. The pathogenesis is gained through molecular interactions between specific microbial proteins and host cells. Leading various changes in the host cell functioning promote the pathogen to invade host cells and tissues causing disease in the host\(^7\).

The term ‘host pathogen interaction’ is a term that informs how the pathogen is interacting with its host, adhering to the appropriate target, invasion, colonisation, making damage to the host and getting transmitted to another host. In short, it can be said that host pathogen interaction helps us to uncover the nature of infection\(^8\). It opens a new scope to study the pathogenicity of the microbe and to develop armamentarium against infectious disease.

This review provides an overview of the survival mechanisms of Mtb and role of host pathogen interaction in establishing the disease. Various aspects of the interaction of the pathogen protein to their receptor on the host are discussed. Better insight of the interaction between the host and pathogen will enable the researchers to identify drug target, explore new techniques and strategies to eliminate the severity and economic impact of infectious diseases.

I. Survival strategies adapted by Mtb inside the host cells:
There are several mechanisms that contribute to the survival of Mtb within the macrophages. The major ones are discussed below:

Preventing the phagosome maturation: Macrophages create first line of defence against the pathogenic bacterium. Macrophages phagocytose the bacteria for its removal by
exposing them to phagosome which provides highly acidic environment and contains hydrolytically active enzymes. *Mtb* has developed the ability to protect itself from macrophages by inhibiting the phagosome maturation process. Phagosome maturation is necessary as this is the critical step of bacterial clearance and antigen processing.

Zinc-dependent metalloprotease-1 (Zmp1) is an important player in pathogenesis of *Mtb* and plays an essential role in inhibiting the phagosome maturation. It inhibits the caspase-1 which prevents the activation of inflammasome, thus averts the processing of the interleukin pro-IL-1β into IL-1β and the consequent phagosome maturation.  

**Pathogen dependent inhibition of the phagosome-lysosome fusion:** Inhibition of the growth and intracellular killing of a pathogen within the mononuclear phagocyte of the host cell are dependent on phagosome-lysosome fusion. It inhibits the phagosome lysosome fusion by blocking the host phosphatidylinositol 3-phosphate (PI3P) which is an essential component of the host membrane helping in phagolysosome biosynthesis. PI3P is a target site of several proteins like the EEA1 (early endosomal autoantigen 1) and the hepatocyte growth factor-regulated tyrosine kinase substrate (Hrs) which are engaged in the maturation of the phagosome into lysosome.

Inhibition of the phagosome-lysosome fusion is achieved via 2-fold strategy: (a) Interfering the activity of PI3P through the blocks the phagosome-lysosome fusion. (b) A second strategy used by the *Mtb* is secretion of SapM (Secretory acid phosphatase), a eukaryotic-like acid phosphatase that prevents the PI3P accumulation on phagosomes by the phosphatase activity resulting in the inhibition of phagosome-lysosome fusion.

**Preventing acidification of the phagosome:** Biological acids play vital roles in eukaryotic immune mechanism, as acidification of the phagosome is a potent antimicrobial host defence. Therefore, pathogens have evolved numerous mechanisms to counteract acid-mediated defence mechanism and to gain access to host resources. For the intracellular survival, *Mtb* requires the stable phagosome acidification around 6.3 to 6.5 pH, which is maintained by multi-subunit and highly conserved protein complex Vacular H+ ATPase. Recent studies suggested that the *Mtb* controls the phagosomal acidification through microbial protein tyrosine phosphatase PtpA which prevents the interaction of V-ATPase to the Mtb-containing vacuole and also through interfering with host suppressor of cytokine signalling (SOSC) protein functions.  

**Protection from oxidative and nitrosative stress:** Host-derived anti-microbial oxygen and nitrogen radical is an immune response which destroys the ingested microbes during inflammation and host defence. In order to survive and persist within macrophages, the suppression of oxidative responses is another defence mechanism adapted by the *Mtb*. Alkyl hydroperoxide reductase (Ahpc) enzyme of *Mtb* combats oxygen radical, detoxifies organic hydroperoxides and degrades superoxide by the two superoxide dismutase (SOD) i.e. SODa and SODc. It was reported that the thioredoxinreductase (TrxB2), a substrate of PtkA phosphorylation, plays an important role in the defence against oxidative stress.  

**II. Mycobacterial protein interactions with the host:** The pathogen *Mtb* has evolved multiple strategies to counter host immunity as discussed earlier. Host–pathogen interaction is another very important factor in virulence and survival of the bacterium. Some of the major interacting proteins are:

**Cell wall Proteins**

**Mycolyl transferase Ag85B:** In *Mtb*, mycolyl transferase is also termed as Ag85 or antigen 85 complex enzyme which is made up of fibronectin-binding proteins: FbpA, FbpB and FbpC2 and these proteins have abilities to bind fibronectin (FN). It is a large adhesive glycoprotein which assists the *Mtb* bacterium to attach alveolar macrophages. It maintains the integrity of the cell wall by synthesising the alpha, alpha trehalose and helps in building the bacterial cell wall by transferring mycolyl residue from one molecule of alpha, alpha-trehalose mono mycolate to another which leads to the formulation of cord factor or alpha, alpha-trehalose di mycolate. They are potent immunoprotective antigen and because of its location at the cell wall and its involvement in the cell wall synthesis, it is considered as a leading drug target.

**Mammalian cell entry proteins:** Mammalian entry protein (MCE) is surface exposed or secreted protein which is organised in the large operons. *Mtb* contains four dispersed but homologous mce operon i.e. mce1-4. Each operon comprises eight genes organized in two yrbE genes (A and B) followed by six mce genes i.e. mceA-F. The name is derived from their property of entering inside the mammalian cells, survival within the macrophage and contributes to *Mtb* virulence.

The YrbE proteins are probable integral membrane proteins consisting of six TM alpha helices and mce1E-4E, which are probable lipoprotein precursors. The Mce genes encode adhesion and invasin-like proteins (Iip) with putative signal sequences at the N-terminal end. It is present in both pathogenic and non-pathogenic bacteria which suggest that the presence of putative virulence gene is not an indicator for pathogenesis of *bacilli*. Recent evidence suggested that Mce proteins are the component of lipid ABC transporter or ATP-binding cassette transporters.

**Porin (OmpATb):** It is characterised as pore forming protein and it facilitates the survival of *Mtb* at low pH inside the phagosome during the infection. OmpATb develops the resistance against acidic environment by getting induced at pH 4.5 and through the acid-induced pore closing. It also neutralises the acidic environment by enabling the
transportation of ammonia in the phagosomal space\textsuperscript{74}. This porin protein plays an important role in pathogenicity.

**Heparin binding hemagglutinin adhesin (HbhA):** To establish any infection by the microbes, adherence to the mammalian host tissue is a very crucial virulence factor. Heparin binding hemagglutinin adhesion is a surface protein which is needed for extrapulmonary dissemination of \emph{Mtb} from lung to spleen. This protein predominantly mediates the binding of the tubercle bacillus to epithelial cells by adhering to the sulphated glycoconjugates on nonphagocytic cells. It promotes the agglutination of the erythrocytes of certain host species. It also induces the mycobacterial aggregation and promotes the mycobacterial colonisation\textsuperscript{51}. HbhA is an immunogenic antigen and previous studies have stated that immunisation with HbhA produces an equal protection like BCG vaccination and can be used as a booster vaccine\textsuperscript{72}.

**Cell envelop proteins**

**Exported repetitive protein (Erp):** Erp protein is also known as P36 protein as its molecular mass is 36 kDa. It is a surface protein of the cell wall and is a crucial virulence factor, comprising of three domains: N-terminal, Central and C-terminal domains. The N- and the C-terminal are similar but central domain harbours several PGLTS motif (Pro-Gly-Leu-Thr-Ser) repeats that differ considerably between mycobacterial species and this variability may relate to the virulence\textsuperscript{38}. After mutation study of \textit{erp} gene and reintroduction into the mutants, it was reported that Erp protein helps in the virulence\textsuperscript{37}.

Although the information of the virulence is known but the exact role of the Erp in the pathogenesis of the \emph{Mtb} is not clear\textsuperscript{20}. The Erp protein is not only present in the pathogenic mycobacterium but is also present in the saprophytes suggesting that Erp plays more than one physiological role\textsuperscript{14}.

**Lipoproteins**

**LppX and LpqY:** Lipoproteins are the major antigens in the \emph{Mtb} that are reported to affect both innate as well as active immunity. Virulence factors, LppX and LpqY plays essential role in host cell invasion, outer membrane integrity and spore germination\textsuperscript{17,26,51}.

LppX and LpqY are 27 kDa membranes associated lipoprotein which helps in translocation of complex lipids. Their crystal structure consists of a U-shaped beta-half-barrel with a large hydrophobic cavity. LppX translocates the phtiocerol dimycocerosates (PDIM) from the cell membrane to the outer membrane of \emph{Mtb}\textsuperscript{71}. This protein is common to \emph{Mycobacterium leprae} and \emph{Mtb}.

LpqY is a part of trehalose ABC transporter substrate-binding lipoprotein of \emph{Mtb} and it forms an operon with sugA, sugB and sugC. Various studies showed that \textit{lpqy} gene is required in the growth of mouse and in macrophages which means sugar molecule could be important for the infection. A study of virulence of the LpqY suggested that this permease is specific for the uptake of the disaccharide trehalose which is not produced by mammals. Trehalose is a biproduct of the biosynthesis of the cell envelope by \emph{Mtb} bacterium’s Ag85 complex or mycolyl transferase\textsuperscript{62}.

The LpqY-SugA-SugB-SugC ATP-binding cassette transporter is highly conserved in mycobacteria which comprises LpqY, the periplasmic sugar-binding lipoprotein; SugC, the ATP-binding protein and the transmembrane proteins SugA and SugB. LppX and LpqY can be a potential drug target\textsuperscript{65}.

**LprG:** LprG is a 27 kDa lipoprotein. It is one of the most studied lipoproteins as it is structurally homologous to the mycobacterial lipoprotein LppX and is characterized by a lipobox motif (LVI/ASTV/GAS/C)\textsuperscript{64}. Studies described that it is also a glycoprotein and is a potent antigen of \emph{Mtb} and \emph{Mycobacterium bovis}.

Lipobox motif initiates the post-translational modifications at the conserved cysteine sites during lipoprotein synthesis and transportation. This modification is directed through serial action of the three enzymes preprolipoprotein diacylglycerol transferase (Lgt), prolipoprotein signal peptidase (LspA) and apolipoprotein N-acyltransferase (Lnt). LprG plays an important role in transport and localization of lipoarabinomannans (LAM), lipomannans (LM) and triacylglycerides (TAG)\textsuperscript{18,25}.

**Protein kinases**

**Protein kinase D (PknD):** It is a 69.5 kDa transmembrane serine/threonine protein kinase which has a C-terminal extracellular domain comprising of six tandem repeats of 40 amino acids. This protein possesses autophosphorylation activity like other serine/threonine protein kinase and shows a complex phosphorylation pattern. The N-terminal regulatory portion has a cysteine-rich domain consisting of a tandem repeat of cysteine-rich, zinc finger like motifs and a pleckstrin homology domain which regulates the catalytic activity. PknD is a novel target site for diacylglycerol (DAG) and phorbol esters\textsuperscript{67}.

**Protein kinase G (PknG):** It is a eukaryotic-like serine/threonine protein kinase (STPK) that mediates the intracellular survival of mycobacteria. This crucial virulent factor blocks the maturation of the lysosome and resists intracellular degradation of mycobacteria within phagolysosomes. PknG is not only required for the growth of mycobacteria but also for its growth within the host macrophages\textsuperscript{69}.

Mycobacterial protein kinases share homology with the eukaryotes and eleven genes code for the eukaryotic like serine/threonine protein kinase. The PknG shows homology to a mammalian protein kinase Ca (Pckα) which implies that the protein kinase G could interfere with host signalling event\textsuperscript{54}.
Out of 11 mycobacterial protein kinase localised in cell membrane and cell wall, PknG is soluble in cytoplasm. PknG is expressed by the pathogenic bacteria like Mtb, Mycobacterium bovis BCG but not by Mycobacterium smegmatis which a non-pathogenic species. This protein kinase facilitates the transfer of signals sensing nutritional stress in pathogenic bacteria Mtb and translate the signals into metabolic adaptation\textsuperscript{11}.

**ATP synthase**

**F0F1 Type ATP synthase**: It is a membrane bound ion channel that is present ubiquitously in all kingdom of life. Mycobacterium leprae, Mycobacterium ulcerans and Mycobacterium tuberculosis (Mtb) reside in human host for several years in dormant state by shifting-down their energy metabolism\textsuperscript{21}. ATP synthase performs synthesis or hydrolysis of nucleotide, usually ATP and controls the movement of ions through membrane. It plays essential role in survival of pathogen under the stress conditions encountered in the human host\textsuperscript{18}. ATP synthase enzymes of Mycobacterium were considered as drug target in the recent years and subunit \(\varepsilon\) of ATP synthase enzyme was validated as drug target for bedaquiline a diarylquinoline. The ATP synthase of Mtb is homologous and similar to other bacterial as well as eukaryotic ATP synthase. The composition of \(F_0\) sector (\(\alpha_1\beta_2\gamma_{10-15}\)) and a hydrophilic \(F_1\) part (\(\alpha_3\beta_3\gamma_6\)) make it unique form others\textsuperscript{28}.

The ATP synthase subunit alpha and gamma were also proposed as a potential drug target in previous studies. The 36 amino acid residues extension ATP synthase subunit alpha and the region of 13 amino acids residues of ATP synthase subunit gamma in Mtb makes it unique from other organisms\textsuperscript{55,58}.

**MgtC protein (mgtC)**: It is a P-type ATPase transmembrane protein and is responsible for \(\text{Mg}^{2+}\) uptake, important for the synthesis of DNA and RNA. It is required to maintain genomic stability as it binds to phosphate group present in the genome\textsuperscript{24}. MgtC plays a key role in replication and growth of pathogen inside the macrophage. Despite being second most abundant element in a cellular system, magnesium is found in less concentration inside the macrophages.

Therefore \(\text{Mg}^{2+}\) uptake is required for the survival of the pathogen Mtb inside the macrophages. MgtC proteins have conserved N-terminal transmembrane domain and a variable domain. Previous studies suggest the dual role of MgtC which depends on whether the bacteria are residing inside host macrophages or in liquid culture\textsuperscript{62}. MgtC is a virulence factor and a key player in the survival of the Mtb as well as several other intracellular pathogens\textsuperscript{1}.

**CtpC transporter**: It is a heavy metal cation P-type ATPase that acts as an exporter for \(\text{Zn}^+\) and used by mycobacteria in defence mechanism for its survival for long period of time within human macrophages. Zinc is essential for the growth of bacterium, but its high concentration can be lethal. *Mtb* bacterium comprises of 11 ctp genes, ctpA-J and ctp V which encodes the protein that is predicted as probable cation transporters P-type ATPase or P-type ATP synthase. They have auto-hydrolytic ATP activity required for metal transport.

Previous studies have reported that human macrophages use heavy metal toxicity as a mechanism of antimicrobial defence. A sudden increase in concentration of the \(\text{Zn}^{2+}\) was noticed after few hours of mycobacterial infection but it has been seen that P1-type ATP synthase neutralizes the poisonous effect within macrophages by draining out the excess zinc metal ions outside the mycobacterial cell\textsuperscript{7}.

**Drug Targets identified through Host Pathogen interaction analysis**: We have already discussed some of the strategies that are adopted by the *Mtb* to survive inside the host macrophage. The virulence factors of the bacterium interact with the proteins of the human host and establish the infection. The understanding of Host Pathogen Protein-Protein Interactions (HP-PPIs) will help the researchers to develop new tools and strategies for exploration of novel drug targets and to eradicate the disease\textsuperscript{15}. The molecular cross-talks between the host and their pathogens are mediated by HP-PPIs.

The pathogenic hijacking or rewiring helps the bacterium to grow in the adverse environment and survive against various immunological responses. The rewiring or hijacking may be carried out by range of mimics that resemble the proteins of the host in both form and function\textsuperscript{16}.

Several experimental techniques have been developed to date for investigating protein–protein interactions viz. biochemical methods, biophysical and imaging techniques and computational methods\textsuperscript{1,23,50}. Now it has become quite easy to study the protein–protein interaction (PPI) network as around half a million of the interaction are indexed in the database. There are several methods to explore and analyse the PPI network. Walhout and his team\textsuperscript{78} had introduced the homology protein mapping or interologs method to find out the unknown interactions. According to this method two proteins C and D are said to have functional linkages if they have higher homology with the pair of interactive proteins A-C and B-D that have been experimentally verified (Figure 1).

\begin{figure}
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\includegraphics[width=0.5\textwidth]{fig1.png}
\caption{Schematic representation of protein-protein interologs}
\end{figure}
Before this approach, many attempts were made to predict the protein interactions; protein docking approach is one of them\(^4\). Another approach uses sequence data of the interacting protein interface to predict the interaction profile\(^3\).

Logical modelling framework designed by the Franke et al\(^5\) was important study in the field of computational biology that directs the host pathogen interaction analysis and predicts how the pathogenic bacteria changes the signalling pathway in the host. The study identified the potential novel therapeutic target to prevent the pathogenic effects in *Helicobacter pylori* infection. Raman and Chandra\(^6\) designed a genome-scale interactome network for the *Mtb* H37Rv strain. Pathway analysis was performed and a new concept of ‘co-target’ was anticipated for combating drug resistance. Potential drug targets were identified from the co-targets e.g. Rv0823c, DnaE1, RecA and Rv0892 which target the metabolic pathway. In the same year Raman et al\(^7\) designed a target TB, pipeline in which interactome, reactome and genome-scale structural analysis was done to identify drug target that may help in the drug discovery process. With this pipeline, 451 drug targets were identified that are non-homologous to host target and gut flora.

Raman and his team\(^8\) are continuously working on development of different strategies from the machine learning approach, subgraph mining and now predicting the synthetic lethals in the metabolic network through Fast-SL algorithm to decipher pattern of PPI network between *Mtb* and its host. Mathematical and computational approach was adopted to study interactions between *Mtb* and the human immune system. The importance of computational approach to study host pathogen interaction was also discussed.

The study describes how the mathematical and computational models can be used to mimic biological system and this can be a powerful tool to study host pathogen interactions. The mathematical and computational models which allow the researcher to understand the framework of the experimental system, perform *in-silico* experiments like virtual knockouts and deletion, prediction of new therapies and vaccine targets and many more\(^9\).

PPI network of H37Rv strain of *Mtb* was built through homogenous protein mapping method. The study suggested that ribosomal proteins, ABC transporters and molecular chaperones are interconnected proteins. An unknown, protein kinase (PknK) and the hypothetical protein (Rv1354c) were predicted to have interaction with ABC transporters. The Rv1354 gene was known to be the cause for the turnover of messenger molecule cyclic-di-GMP in *Mtb* H37Rv.

A hypothetical protein, Rv2752c was characterised as a metal-beta-lactamase\(^10\). Tuberculist (http://tuberculist.epfl.ch/), a database containing genome derived information of H37Rv which was used since last decade but the updation of the database has not been done. The study suggested that the advancement in post-genomics era has affected our understanding of *Mtb* biology significantly and facilitated subsequent drug target identification and validation.

Interactions between pathogen and host proteins allow pathogenic microorganism to manipulate host mechanism in order to use host capability and to escape from host immune response. The result of infection with *Mtb* is largely affected by the host–pathogen interaction in which both the human host and the *Mtb* genetic backgrounds play an important function\(^11\). Rapanolo et al\(^12\) used interlogs method for predicting the inter species interaction between human and *Mtb*. The subcellular localisation of the protein was involved in study to check feasibility of the predicted interactions.

871 potential drug target proteins were identified and out of which 4 *Mtb* proteins i.e. dnaB, fadD13, rlmn and hemL, interacting with CD74 or HLA class II histocompatibility antigen gamma chain are predicted as potential drug targets\(^13\). Another study proposed three targeted proteins that are essential for the growth and survival of the *Mtb* CDC1551 strain. The targets of these proteins are L-lysine 6-monoxygenase and mbtG which is assumed to have role in lipid metabolism. Rv0227c a conserved membrane protein and Rv0102/MTO111 an uncharacterized protein, both are involved in cell wall and cell processes\(^14\).

Previously, the conventional homology-based interlogs method was one of the methods used to identify inter-species or intra-species PPIs. A new stringent homology-based method was developed by Zhou et al\(^15\) which uses the experimental HP-PPI template for finding direct physical PPI. Using this approach 1005 *Homo sapiens-Mtb* H37Rv PPI was identified. This study provided better strategy in identification of PPI between eukaryotic host and prokaryotic pathogen in comparison with conventional homology-based approach.

Based on meta-analysis, data mining and *in-silico* analysis, 54 potential protein targets are essential for the survival of the pathogen and are non-homologous to host or gut flora. Subtractive genomics approach was adopted for finding novel drug target. Mce-family lipoprotein, lipoprotein (LprO, LprG, LprH, LppI, LppM, LppP etc.), probable cutinase Cut2, PPE family protein PPE6 were some of the proteins suggested as potential drug target in the study\(^16\).

Huo et al\(^17\) predicted the host pathogen interactions (HPIs) between *Mtb* H37Rv strain and human based on sequence motifs. The study used the Interolog method and domain-domain interactions (DDIs). 118 pairs of the Host pathogen interaction were identified and PATH database was developed which is the specialized database for HPIs on *Mtb*\(^17\). Protein structure similarity was studied by some of the researchers to predict interaction between host and pathogen. Pairwise sequence similarity protein-protein...
interaction (PSS-PPI) method uses heteromeric protein complex structures stored in the PDB (www.rcsb.org) database.

The human and Mtb, PPI network was constructed. But the only drawback of this method is that there were several proteins that do not have well-defined 3D structures. The study suggested that the ESAT-6 secretion system (ESX) family, serine/threonine protein kinase (STPK) family and the PE/PPPE family proteins of Mtb show interaction with human proteins and were responsible for immune response and phagocytosis pathways. This finding can serve insight in identifying potential drug target and development of anti-tubercular drug\textsuperscript{13}.

Another study using the PDB structure was performed by the Mahajan and Mande\textsuperscript{13}. Structural knowledge available in the protein data bank was used to identify the host microbe interaction. Domain-domain interaction (DDI) information in PDB complexes was utilised to score and prioritize candidate PPIs between host and pathogen proteomes based on targeted sequence-level comparisons\textsuperscript{13}.

Random forest model, a machine learning approach was used to generate bacteria-host protein interactions via known bacterial protein interaction networks. This method will explore new potential drug targets, will find alternative solution to drug resistance and reveal the interaction pattern of Mtb H37Rv protein to human\textsuperscript{47}.

Conclusion

The invasive infection of the Mtb and host immune response is fundamental to understand the pathogenesis of the bacterium and discovery of therapeutic drug target. The current review showcased the way Mtb attack its host, the protein altered by the Mtb responsible for perturbing normal functionality of host, the gene coding these proteins and survival mechanism of bacterium inside a host. Recent scientific research studies showing improvement in host pathogen interaction study were reviewed and the potential protein targets were cited in this study.

The knowledge of the survival mechanisms and the host pathogen interactions will improve the understanding that how the Mtb bacterium infects the host and makes it able to survive inside the harsh environment of host. The gaps identified are: (a) All the host pathogen interactions analyses have been done till now on single strain of Mtb. (b) No comparative studies have been performed yet between different strains of the Mtb and human host, which may help researchers to identify common and effective drug target. (c) Docking analyses of the target proteins obtained from host pathogen interaction analysis were not performed yet; this can help the researchers to identify the binding pocket of the target and in drug discovery process.

Bioinformatics approach may allow us to analyse and elucidate the host pathogen interaction between Mtb and human host. This will further enhance our insight on survival of mycobacterial cells inside the human host and reveal the novel aspects of host cell biology. Ultimately such insight might help us in designing new drugs to control TB.

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References


79. http://apps.who.int/iris/bitstream/handle/10665/274453/9789241565646-eng.pdf?ua=1 Accessed 02 April 2019


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