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# Proteomics and Bioinformatics: A Modern Way to Elucidate the Resistome in *Mycobacterium tuberculosis*

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## Present Status

Tuberculosis (TB) remains one of the world's biggest threats which are caused by *Mycobacterium tuberculosis*. According to WHO 2016 report, 10.4 million people were infected worldwide with 1.8 million deaths including 0.4 million individuals with HIV-TB co-infection [1]. Vaccines, diagnostics and drugs are the available current tools to control this situation. Over the half century, Mycobacterium bovis bacille Calmette Guérin (BCG) is still the only vaccine against TB worldwide, despite showing highly variable efficacy (0–80%) in different trials [2]. Worldwide, sputum smear microscopy and culture remains the commonly used TB diagnostic and gold standard method respectively. However, use of rapid molecular testing like Line Probe Assay (LPA) has been used for detection of Rifampicin and isoniazid drug resistant *Mycobacterium tuberculosis* strains. Recently in India, Revised National TB Control Programme (RNTCP) has approved a study for the Validation of second line LPA for detecting resistance to fluoroquinolones, aminoglycosides (kanamycin, amikacin) and cyclic peptides (capreomycin). First and second line anti-TB drugs are effective and necessary component of short course chemotherapy. The treatment failure can lead to the emergence of resistant strains [Multidrug-resistant Tuberculosis (MDR-TB), Extensively Drug Resistant Tuberculosis (XDR-TB) and Totally Drug Resistant Tuberculosis (TDR-TB)] and consequently spread of the resistant form of the disease which have worsened the situation and became a major threat to community. The reasons for this are complex and multifactorial. These drug resistant *M. tuberculosis* strains or bad bugs can resist the action of drugs by the various mechanisms. These includes target gene mutations [3], drug modifying enzymes [4], over expression of efflux pumps and porins alterations [5,6], drugs trapping and overexpression of proteins showed drug neutralizing effects [7-13]. Majorly of drug resistance is contributed by target gene mutation however remaining part of drug resistance is due to various other mechanisms. Our existing gadgets (vaccines, diagnostics and therapeutics) are incapable to provide the complete protection against these deadly situations.

## Discovery and Targeted Proteomics Coupled with Bioinformatics Approaches: A Modern Way to Elucidate the Resistome

Since the last decade most of drug resistant proteome reports based on the discovery (expression proteome) and targeted proteomics coupled with bioinformatic approaches have been accumulated [7-24] which suggested that proteomics along with bioinformatics approaches are the modern tool to explore the mystery of resistome in addition to known factors. In the discovery/expression proteomics two-dimensional gel electrophoresis (2DE) and mass spectrometry are the best tools for separations and identifications of proteins which are the potential factors for virulence and resistance. Further the bioinformatic studies (like interproscan analysis, molecular modeling and docking, pupylation analysis and protein-protein interactions) of these potential virulence and resistance factors supported their involvements in virulence and drug resistance. In our previous studies we have reported a panel of proteins (functionally known and unknown/hypothetical) by proteomic and bioinformatic approaches and suggested their roles in virulence and resistance. Further in depth studies of these proteins and their associated pathways could suggest their use as markers or drug targets against resistant tuberculosis.

## Proteomics and Bioinformatics Explored New Strategies to Fight against Resistance: In the Antibiotic Resistance Era

Proteins are important because it displays the real state of the cell and could be the potential factor involved in resistance and virulence. Firstly, these proteins might be used as future diagnostic markers against resistance which is the part of diagnostic strategy. Secondarily, these proteins and their pathways could be the potential drug targets against the resistance which is the part of drug targets strategy against resistance. Thirdly, stress proteins, cell wall and membrane related proteins are the key virulence antigens which are expressed during any stress (such as drug) and needed for attaching, entering and surviving in different cellular microenvironments. These proteins (virulence factors) could lead to the development of ant virulence factors and elucidate the antivirulence strategy against this deadly situation.

### Conflict of Interest

There is no conflict of interest between the authors.

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