

Synthetic Genomics to ‘Unmasking the Masquerades’ as Potential Vaccine Biomarkers in Multi-Drug-Resistance *Mycobacterium tuberculosis* (MDR-TB)

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Death tolls due to *Mycobacterium tuberculosis* infections remained increasingly high despite an intensive global fight against TB. Biomarkers are measurable indicators that can be used to diagnose or monitor disease progression which are usually host and pathogen-derived.

The Bacillus Calmette-Guerin (BCG) vaccine; the only licensed vaccine continued to exhibit its flawed inconsistency, hence the need for more potent TB vaccine. Attention is widely shifted to several hidden immunogenic and antigenic shift to surface-exposed proteins ‘the masquerades’ of *M. tuberculosis* which allows the organism to evade immune responses and help them survive as intracellular in macrophages, cytosol and phagolysosome. The current norms of six to eight months TB regimen of first-line anti-TB treatment are no longer effective for persons with MDR-TB and XDR-TB. For over a century, the only authorized TB vaccine against TB strains is *M. bovis* derived Bacillus Calmette-Guerin (BCG) vaccine in which BCG is a live and attenuated form of the bacterium. Unfortunately, BCG vaccine does not provide enough protection against the most common form of the disease which is pulmonary tuberculosis in adults. This is largely due to high genetic variability of the bacteria, lack of understanding of the immunological responses to combat MDR-TB. Another limited success of the past researches includes inability to progress well during clinical trials of various vaccine candidates and perceived high cost and accessibility; particularly in resource-limited settings where MDR-TB is most prevalent.

The future of TB threat depends on aggressive vaccines design aimed at preventing the infection by *Mycobacterium tuberculosis*; offers long term protection, having population-level impact, it breaks transmission cycle, it is the most cost effective as well as offering complementary functions to drugs therapy.

Recent innovations in genome-based technology, such as extensive genomic, transcriptomics, and proteomic analysis; rapid identification of novel vaccine against MDR-TB within the shortest possible time is more feasible than ever before. This ‘genomic era’ has prompted a paradigm shift in vaccine development which sped up the process of vaccine development as we see in the case of mRNA vaccine developed for COVID-19.

Beyond genome-based approaches for the development of vaccines lies the newest synthetic genomics which is a nascent domain of synthetic biology concerned with the creation of living organisms using genetic material. In this field, genes, chromosomes, gene networks, and whole genomes are combined with the help of computational approaches for chemical DNA synthesis [1].

In the soonest future, efforts should be on the synthetic genomics approach to generate drug analogs that can be used to treat other dangerous types of MDR-TB, such as extensively drug resistant TB(XDR-TB) and totally drug-resistant TB (TDR).

Bibliography

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