

Use of Biomarkers in Tuberculosis Treatment: A Challenging Approach

Jagadevappa Patil*

VT's Shivajirao S Jondhle College of Pharmacy, Asangaon-421 601, Shahapur, Thane, Maharashtra, India

*Corresponding author: Jagadevappa Patil, VT's Shivajirao S Jondhle College of Pharmacy, Asangaon-412 601, Thane, Maharashtra, India, Tel: 9448816812; E-mail: pharmajspatil@gmail.com

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Introduction

The ultimate success of any kind of chronic disease treatment depends on relapse chances. Therapy of infectious diseases like tuberculosis (TB) presents many hurdles in spite of much advancement achieved in the drug discovery and novel drug delivery strategies. Presently success of TB treatment is measured based on its relapse within two years after the treatment period. Pharmaceutical industries are un-attracted to develop new anti-TB molecules due to consumption of longer duration of clinical trials. Biomarkers may assume to be shortening the clinical trial period. Presently there is deficiency of adequately validated biomarkers and their appraisal in prospective clinical studies. Premature assessment of the retort to TB treatment may advance regular clinical management and evaluation of new anti-TB molecules. Discovery of new anti-TB molecules are immediate need as the existing molecules are age old and suffering with many limitations. Current TB therapy requires a minimum of six months duration with increased incidence of multidrug resistant bacteria has been reported [1-4]. Clinical management of TB depends on patient adherence and thus treatment out. Response of individual patients differs and early response to the treatment may require a shortened course of therapy [5,6]. Therefore, different patients require different duration of treatment and hence, health care providers may be able to spotlight more concentration on patients who have a high risk of treatment and outcome. Hence, it necessitates substituting biomarkers that offer signs of treatment efficacy. These biomarkers would not only enhance therapeutic strategies and perhaps minimize drug resistance, but also be decisive in validation of new Anti-TB molecules thereby speeding new drug development through reducing of clinical trial process. Conventionally the treatment response for TB is measured based on decrease in mycobacteria in sputum. However, detection of mycobacteria from sputum culture is properly validated as adequate marker. The only accepted biomarker for sterilizing activity is conversion to negative sputum culture at month two of treatment [7].

Antigens and Antibodies as Biomarkers

Several studies have been reported on the role of mycobacterium tuberculosis antigens as biomarkers for treatment response and outcome. The level of mycobacterial antigen 85 in sputum at the beginning of treatment showed treatment success and continued expression of antigen 85 associated with relapse. It has also demonstrated that antigen 85 could be potential biomarker for assessment of new anti-TB molecules [8,9]. In the similar way antigen 85B m RNA levels are pinpointing the treatment response and relapse [10]. In addition the severity of infectious disease connected with antibody levels and titres to two mycobacterial enzymes before therapy directly correlated with failure of treatment [11].

Immune Products as Biomarkers

Many laboratories have conducted studies on role of different immune products as biomarkers during active TB and its therapy. Though these immune products are not specific for TB and are detected even in other infections, few of them have been shown to be associated with severity of disease and/or treatment response. IFN γ detected and measured in sputum has been associated with treatment response and bacterial clearance, [12] and sTNF-R1 and 2 with granzyme B have been associated with sputum conversion [13]. These biomarkers are shown to be treatment sensitive but no evidence about their usefulness in predicting treatment outcome.

Conclusion

To accelerate the drug discovery process for TB treatment it is necessary to develop new substitute biomarkers that can offer detection of treatment efficacy and clinical prognosis. Bio-products detected in serum without further *in-vitro* exploitation would offer the best biomarkers. Such validated biomarkers can help in developing new therapeutic strategies and also possible to reduce the drug tolerance and resistance additionally render speedy and shortened clinical trials of new anti-TB molecules. Presently much attention is given by the World Health Organization (WHO) in collaboration with many international research foundations to find out such biomarkers. It is very much essential to urgently be prioritizing the pursuit of this research area in order to improve the TB chemotherapy and control of the TB pandemic.

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