The Success Story of Private–Government Collaboration to Develop a Rapid Diagnostic Test for Tuberculosis: A Major Public Health Problem in India through a Research Grant by Private Funding Organization (Chennai Willingdon Corporate Foundation, Chennai)

Dr. K. Lily Therese and Dr. H.N. Madhavan

The research project started on 1 December 2009 in collaboration with the Institute of Thoracic Medicine, Chetput, Chennai represented by Dr. N. Meenakshi and R. Sridhar with a research grant approved by Chennai Willingdon Corporate Foundation, Chennai. The entire study period was 4 years and 4 months (December 2009–March 2014). This was the first collaborative research work.

The main objectives of the project are

1. To apply the molecular biological technique reverse transcriptase PCR (RT-PCR) targeting 85B gene to rapidly detect the viable Mycobacterium tuberculosis directly from clinical specimens.
2. To detect resistance to first- and second-line drugs using phenotypic method (BACTEC system).
3. To rapidly identify the multidrug resistant (MDR) M. tuberculosis (typically resistant to the two important first-line drugs rifampicin and isoniazid for treatment of tuberculosis) circulating in Chennai population by application of genotypic methods.
4. Detection of viable M. tuberculosis genome from freshly collected clinical specimens by RT-PCR targeting four genes (icl2, hspR, rRNA1P and 85B).
5. Whole genome sequencing of drug resistant M. tuberculosis strains using Ion Torrent personal genome machine.

RT-PCR targeting 85B gene was optimized and applied on the respiratory specimens obtained from clinically suspected tuberculosis patients for the detection of viable M. tuberculosis which is being offered as a routine diagnostic test at SN Referral Laboratory. The PCR-based DNA sequencing to find out novel mutations as well as reported mutations targeting the genes that code for first- and second-line anti-tuberculosis drugs has been done. Out of the 354 M. tuberculosis isolates, 94 (26.5%) were resistant to streptomycin, 73 (20.6%) to isoniazid, 58 (16.3%) to ethambutol, 97 (27.4%) to pyrazinamide and 24 (6.7%) to rifampicin. PCR-based DNA sequencing targeting the genes coding for drug resistance did not show the presence of mutations in 57 (58.7%) PZA, 94 (100%) STR, 25 (31.2%) INH, 51 (87.9%) EMB and 15 (48.3%) RIF resistant strains. A total of 1053 sputum and respiratory specimens (853 clinically suspected tuberculosis patients’ specimens and 160 controls) were processed in the study. None of the control specimens were positive for isolation of M. tuberculosis, and there were 354/853 (34.7%) respiratory specimens positive for the isolation of M. tuberculosis by BACTEC culture. Of the 354 M. tuberculosis isolates, 18 (2.1%) were MDR tuberculosis (MDR-TB--resistant to rifampicin and isoniazid of first-line anti-tuberculous drugs). There were both novel (not reported earlier in the literature) and reported mutations (changes in the gene sequence) targeting the genes that

Figure 1: Photograph with Chennai Willingdon Corporate Foundation Board Members while receiving the first cheque from Mr. Narayanan.
code for resistance. The novel mutations detected in the study will form the basis for the development of new diagnostic kit for the detection of MDR-TB circulating in the local population.

Phenotypic drug susceptibility testing for second-line drugs was standardized for the first time in a private laboratory (through the present project) in Chennai. This study also is expected to result in generating the useful data to find out “the signature sequences” present in the local M. tuberculosis strains to develop rapid diagnostic tests for the detection of drug-resistant M. tuberculosis genome directly from clinical specimens in Chennai population. This is the first research project of its kind in India to apply the molecular biological technique (RT-PCR) for detecting viable M. tuberculosis directly from clinical samples to aid in rapid diagnosis and initiation of appropriate treatment at the earliest.

This is the first study from a private research institution in Chennai to work on whole genome sequencing of M. tuberculosis isolates including MDR-TB, XDR-TB, poly-resistant TB and monoresistant TB strains. The data generated from the study will be useful to unravel the newer drug targets for resistant strains of M. tuberculosis.

We are grateful for the financial support by Chennai Willingdon Corporate Foundation (CWCF), Chennai, and acknowledge the financial support in the form of research grants in all our publications so far. In addition, we have named the sequenced strains of M. tuberculosis deposited in GenBank with the name CWCFVRF MDR 670, CWCFVRF PRTB 19 and CWCFVRF XDR 234.

This is the first research grant obtained from a private funding organization with the social responsibility of developing a rapid diagnostic test for tuberculosis. The collaborators from the Government Hospital were fully involved in the progress of the project providing us with the relevant patients’ samples and the required support throughout the project study period.

**RNTCP Recognition by Government of India**

In order to utilize the molecular biological tests for poor patients in rural areas through primary health centres for rapid detection of viable M. tuberculosis and also isolation of M. tuberculosis and performing phenotypic antibiotic sensitivity for first-line drugs by BACTEC system, we have applied for Revised National Tuberculosis Control Programme (RNTCP) recognition. This is the first non-governmental organization from Chennai who received RNTCP recognition to serve the poor people of India.

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**Publications from the Study**


**Figure 2:** Photograph taken with the Board members after the final presentation of the project.


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