BCIL *seeks partners to license…*

Mycobacterium tuberculosis Protein Tyrosine Phosphatase as potential drug targets for Tuberculosis

Biotech Consortium India Limited (BCIL) is seeking companies interested in developing therapeutics based on Mycobacterium Protein Tyrosine Phosphatase enzymes - MptpA and MptpB (potential drug targets for Tuberculosis). The technology has been developed at the Department of Biochemistry, University of Delhi South Campus, New Delhi, India, keeping in view the urgency for the identification of drug targets and development of drugs based on these targets for curing tuberculosis, which remains a continuous health threat across the globe.

ABOUT BCIL:

BCIL was incorporated as public limited company in 1990 under the Indian Companies Act 1956. It is promoted by the Department of Biotechnology, Government of India and is financed by several all India Financial Institutions, venture capital funds and the corporate sector. BCIL has been actively involved in technology transfer, project management, consultancy, intellectual property services, information dissemination and manpower training related to biotechnology over the last two decades. BCIL has transferred more than 15 technologies in the last 5 years using its expertise in facilitating licensing agreements that allow healthy and productive cooperation between the inventor and the licensee.

BACKGROUND:

Tuberculosis has been a continuous threat for global health. One third of world's population is infected with *M. tuberculosis* asymptomatically. There have been around 2 million deaths every year due to this dreaded disease. The current treatment of the disease usually involves combination chemotherapy based on isoniazid, pyrazinamide, rifampicin and ethambutol. In general, 6 months long course is required for effective treatment of tuberculosis, which often results in poor compliance on the part of the patients, who stop taking drugs as soon as they start feeling better. This leads to development of drug resistant forms of bacilli, which are able to survive routine drug therapy. The ability of *Mycobacterium tuberculosis* to develop drug resistance for the existing drugs being used for the treatment of tuberculosis infection has necessitated the development of new drugs. This has subsequently necessitated the search for potential drug targets for the development of new drugs for the effective cure of tuberculosis.

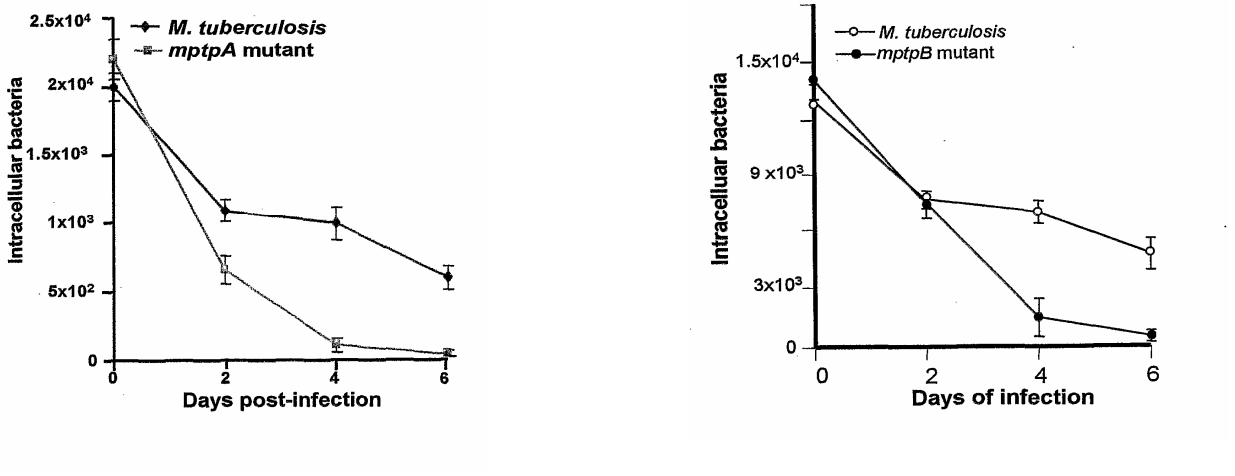
The secreted protein tyrosine phosphatases MptpA and MptpB of *Mycobacterium tuberculosis* are essential for persistence of mycobacterial infections. Disruption of these genes severely impairs the ability of the mutant strains to survive both in IFN-γ activated murine macrophages and guinea pigs. Therefore, the present technology offers these enzymes as the potential drug targets for tuberculosis.

SALIENT FEATURES OF THE TECHNOLOGY:

- The technology offers MptpA and MptpB genes as well validated drug targets as validated in murine macrophages and guinea pigs.

  - Scientists identified the role of protein tyrosine phosphatases (MptpA and MptpB) in the pathogenesis of *Mycobacterium tuberculosis*.
  - They developed recombinant vector comprising the mutated MptpA and MptpB which was used to develop the mutant strains of mycobacteria.
  - Mycobacterium strains harbouring a modified Tyrosine phosphatase gene (MptpA or MptpB) were developed wherein the mutant Mycobacterium strain was found incapable of expressing the active tyrosine phosphatase.
  - Disruption of these genes severely impaired the ability of the mutant strains to survive both in IFN-γ activated murine macrophages and guinea pigs.

(a) **(b)**



(i) Survival curve for wild type and mptpA mutant strain of *M. tuberculosis* in activated macrophages.
(j) Survival curve for wild type and mptpB mutant strains of *M. tuberculosis* in activated macrophages.

Reference: Figure 2B and Figure 8B from the inventors' PCT application published as WO 2005/005639 A2.

APPLICATION/ USE:

- These secretory enzymes represent potentially attractive targets for the development of new anti-tubercular drugs for therapy of tuberculosis.

PATENTS:

- A PCT application (PCT/IN04/00203) was filed with national phase entries in the US, EP, Brazil, Japan and Singapore drawing priority from an Indian patent application (Application no. 882/DEL/2003).

- The National phase-US application has been published recently as 20090215031A1 on 27-08-2009.

- The National phase -EP application has been published recently as 2004770668.

- The National phase -Singapore application has been granted on 31-08-2007.
