

More Medicines for Tuberculosis (MM4TB)

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Research Areas



Basic Research



Product Development

Drugs

At a Glance

- Status: **Active Consortium**
- Year Launched: **2011**
- Initiating Organization: **European Commission Seventh Framework Programme (FP7)**
- Initiator Type: **Government**
- **Rare** disease
- Location: **Europe**

Abstract

Every year, 1.8 million people worldwide die from tuberculosis (TB). Today's TB drugs are nearly 50 years old and must be taken for six to nine months for drug-sensitive disease and up to 24 months for drug-resistant disease. Long, demanding treatment schedules prove too much for many patients, and the resulting erratic or inconsistent treatment can result in drug resistance, treatment failure, or death. The More Medicines for Tuberculosis (MM4TB) research consortium has been assembled to discover anti-infective agents that will combat TB. Evolved from the Sixth Framework Programme project, New Medicines for TB (NM4TB), which successfully delivered a candidate drug for clinical development two years ahead of schedule, MM4TB will apply an integrated approach that includes tripartite screening strategies and medicinal chemistry, functional genomics, and structural biology. This combination of approaches is a broad strategy to discover new compounds, perform pharmacological validation, identify targets, and analyze a variety of mechanisms of action during *Mycobacterium tuberculosis* (Mtb) infection.

Mission

An integrated approach will be implemented by a multidisciplinary team that combines some of Europe's leading academic TB researchers with two major pharmaceutical companies and four small to medium-sized enterprises (SMEs), all strongly committed to the discovery of anti-infective agents. MM4TB will use a tripartite screening strategy to discover new hits in libraries of natural products and synthetic compounds, while concentrating on both classical and innovative targets that have been pharmacologically validated. Whole cell screens will be conducted against Mtb using in vitro and ex vivo models for active growth, latency, and intracellular infection. Hits that are positive in two or more of these models will then be used for target identification using functional genomics technologies including whole genome sequencing and genetic complementation of resistant mutants, yeast three hybrid, click chemistry, and proteomics. Targets thus selected will enter assay development, structure determination, fragment-based and rational drug design programs; functionally related targets will be found using metabolic pathway reconstruction. Innovative techniques, based on microfluidics and array platforms, will be used for hit ranking, determining rates of cidality, and confirming mechanism of action. Medicinal chemistry will convert leads to molecules with drug-like properties for evaluation of efficacy in different animal models and late preclinical testing.

MM4TB will employ novel whole cell and phenotypic approaches for Mtb in conjunction with a prioritized list of validated targets, seeking to generate novel drug leads. A major objective of this initiative is to validate at least five new drug targets pharmacologically and discover at least one family of candidate drugs (CDs). These CDs can be transferred to biotechnology companies or pharmaceutical partners for further development. The involvement of two leading pharmaceutical companies in MM4TB is a major asset; in its previous form as NM4TB, the consortium successfully discovered the benzothiazinone (BTZ) series, which is now in the late stage of preclinical development.

Financing

MMTB is funded through the European Union's Seventh Framework Programme.

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<http://www.mm4tb.org/>

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