TUBERCULOSIS

Mycobacterium tuberculosis W-Beijing genetic diversity
Differential virulence and host immune responses

TB-VIR

A Euro-Asian Research Network on Tuberculosis

TB-VIR is a European research network (Collaborative Project) supported by the European Commission under the Health Cooperation Work Programme of the 7th Framework Programme.

COOPERATION

Context

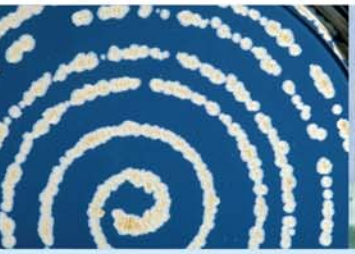
Tuberculosis (TB) is one of the major diseases pointed by the 8th Target of the United Nations Millennium Development Goals which aims to "have halted by 2015 and begun to reverse the incidence of malaria and other major diseases". Indeed, despite tremendous efforts to fight this disease, TB remains a major health problem worldwide and particularly in low-income developing countries.

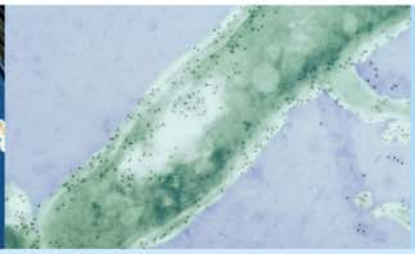
Tuberculosis causes over 1.5 million deaths annually worldwide, and up to one third of the global population is estimated to carry latent *Mycobacterium tuberculosis* infection.

Only 5 to 10% of individuals infected with ***M. tuberculosis*** develop TB. Environmental factors probably play an important role in this phenomenon, but it is increasingly thought that the virulence and load of the infecting strain together with host genetic factors contribute to such differences between infected individuals.

On the pathogen side, the W-Beijing lineage is one of the predominant *M. tuberculosis* families, in terms of morbidity and mortality, worldwide. Strains of the W-Beijing lineage are responsible for 80 to 90% of TB cases in China, where notification rates of active TB is 74 per 100,000 in average (27 per 100,000 in the Shanghai area) and are frequently associated with resistance to antimicrobial drugs, raising concerns about a possible future epidemic of virtually untreatable TB.

The findings of the TB-VIR project will greatly increase our understanding of ***M. tuberculosis*** / host interactions by identifying the genes differentially expressed or regulated in response to various clinical isolates of ***M. tuberculosis*** with an emphasis on genes involved in the immune response. In addition, ***M. tuberculosis*** genes required for macrophage parasitism will be identified.





Objectives

The predominance of the W-Beijing lineage probably results from genetic advantages, including unidentified virulence factors and the induction or modification of specific host cell responses not yet thoroughly investigated.

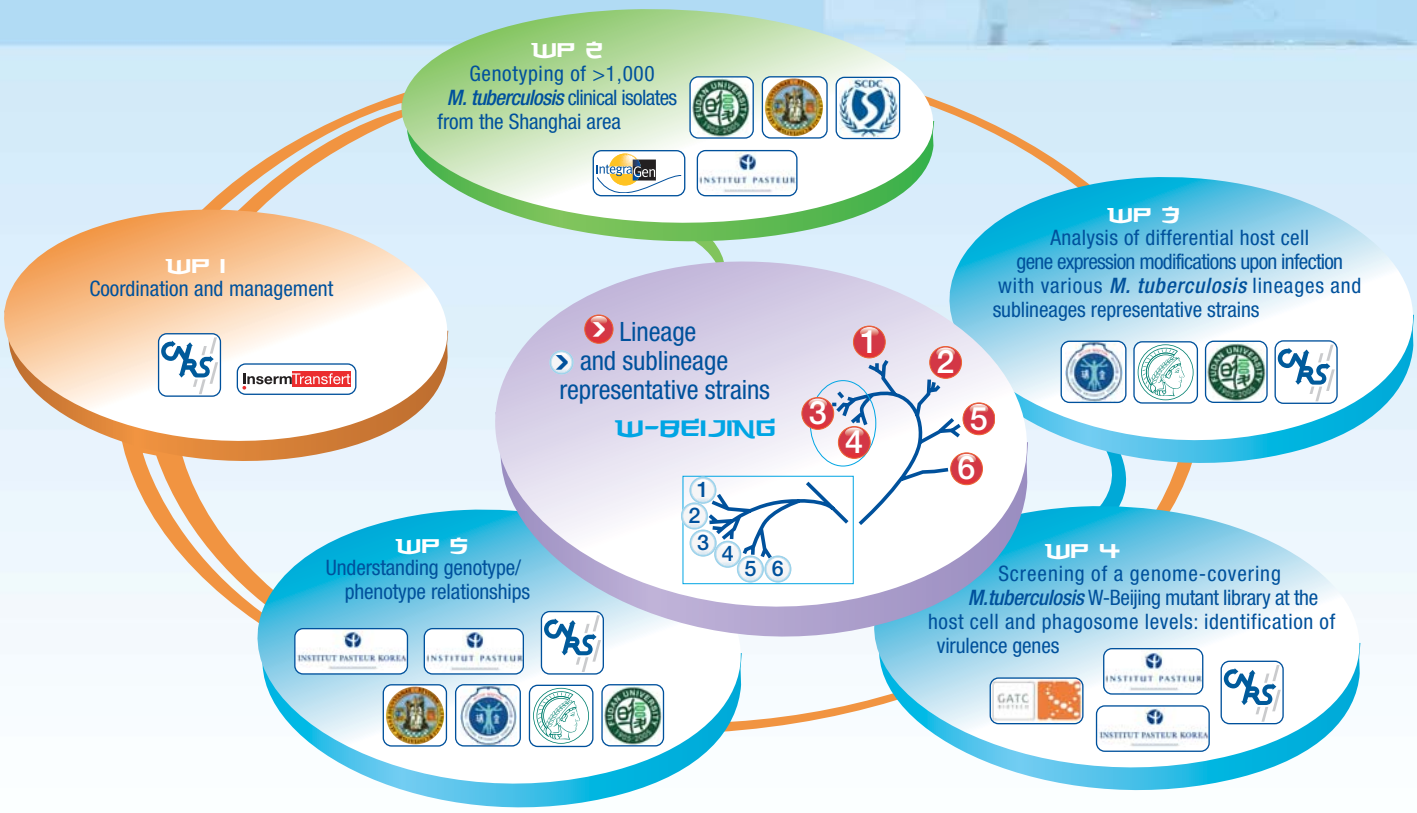
By increasing our understanding of the links between differential host immune responses to ***M. tuberculosis*** infection and ***M. tuberculosis*** genetic diversity and virulence within the W-Beijing family, and between the W-Beijing family and other ***M. tuberculosis*** families, we will improve our understanding of the epidemiological success of this particular lineage. Our results will ultimately lead to the development of novel types of control strategies and of new tools for rapid and accurate diagnosis and intervention for the benefit of the patients.

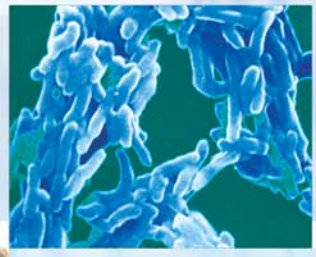
Strategy

The TB-VIR strategy is organized around 5 complementary work packages (WP) focusing on:

1. Ensuring the general coordination of the activities and the smooth communication between the partners of the TB-VIR consortium, as well as the dissemination of the results generated by our activities outside the network, benefiting in an optimal manner to the research community and the patients.
2. Exploring the genetic diversity among the W-Beijing lineage and other minor lineages found in the Shanghai area (China), using SNP-based genotyping.
3. Using representative strains identified through WP2 activity for studying and comparing human and mouse host cell transcriptome responses to infection with the various lineages.
4. Identifying virulence genes by global functional genomics in W-Beijing strain GC1237.
5. And finally, using the knowledge generated by WP2-4 identifying genotype/phenotype correlations and designing functional experiments in vitro and in vivo for evaluating the importance of strain genotype in the observed differences in virulence, pathology and immune response.

TB-VIR work packages and partners' contribution





Expected outcomes

- By increasing our understanding of the links between differential host responses and ***M. tuberculosis*** genetic diversity, TB-VIR should contribute to the development of new, more adequate strategies for diagnostic and prognostic at the patient and community levels.
- Furthermore, results generated by this project, notably information on genes differentially expressed or regulated in response to various clinical isolates of ***M. tuberculosis***, and ***M. tuberculosis*** genes required for macrophage parasitism, will be gathered in our publicly available database, a valuable reference for TB research worldwide.

Partners

TB-VIR is a European research network (Collaborative Project) coordinated by the National Center for Scientific Research (CNRS, Dr. Olivier Neyrolles, Toulouse - FRANCE). This consortium brings together 11 partners, including 3 private companies and 8 laboratories, from 3 Member States of the European Union and 2 Asian countries. It is supported by the European Commission under the Health Cooperation Work Programme of the 7th Framework Programme.

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