DETECTION OF TUBERCULOSIS AND INFECTION
BY MYCOBACTERIUM TUBERCULOSIS USING HBHA

THE INVENTION

The present invention concerns methods for:

• in vitro detection of human subjects infected with Mycobacterium tuberculosis but with no clinical symptoms of tuberculosis. It allows the distinction between the latently infected subjects, those who are uninfected and those who suffer from active tuberculosis. The method allows the detection of both recently infected subjects and subjects who were infected several years before performing the test;

• in vitro detection of human subjects presenting pulmonary and extra-pulmonary active tuberculosis

KEYWORDS

• Mycobacterium Tuberculosis
• In Vitro diagnostic Test
• Detection of Infection (identification of latent TB versus active TB)
• Detection of extra-pulmonary disease

THE POTENTIAL APPLICATIONS AND KEY ADVANTAGES OF THE TECHNOLOGY

A patented method to produce well-defined and disease-relevant human cortical neurons to use as reagent in support to drug development processes. It is estimated that one third of the world population is infected with Mycobacterium tuberculosis and that 5-10% of them will develop active tuberculosis during their lifetime. The risk to develop active tuberculosis is higher in different groups of patients: at risk like HIV-infected subjects, patients with end-stage terminal disease, patients under severe immunosuppressive treatment (for autoimmune diseases, after solid grafts etc...), patients under biotherapies, etc.

It is therefore recommended to detect latent Mycobacterium tuberculosis infection mostly in groups of patients who are most at risk to reactivate the infection and to develop active tuberculosis, in order to treat them prophylactically. This can only be done with a test detecting all the latently infected subjects with a high sensitivity, allowing to differentiate them from active tuberculosis, and if possible determining an index risk factor. Such a test is not available on the market.

It is also recommended to treat very quickly any new case of active tuberculosis and the classical diagnosis by isolation of the bacteria often needs several weeks to be positive and often gives false negative results for extra-pulmonary tuberculosis.

The present invention enables:

• Discrimination between latent and active infection,
• Risk Profiling of patients to develop active tuberculosis.
• Extra-Pulmonary Active Tuberculosis Diagnostic

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TECHNOLOGY DEVELOPMENT STAGE

1. Test Validation

The test validation has been in process for more than 4 years within the Hôpital Erasme:

> 96 hours Test on peripheral blood mononuclear cells validated, with ELISA read-out

Publications:
  - 205 patients
  - 23 patients

> 24 hours Test on peripheral blood mononuclear cells validated, with ELISA read-out

Publications:
  - 137 patients
  - 143 patients

Cohorts currently tested:
- HIV-infected patients
- Screening for latent tuberculosis before starting anti-TNF-a treatment
- Screening for latent tuberculosis before solid graft
- Screening of patients with uveitis that may be secondary to Mtb infection

> 24 hours Test validated on lymphocytes collected at the site of infection, with flow cytometry read-out

Publication:
  - 61 patients

2. HBHA antigen Production and Purification

- Size and purity controlled by SDS-PAGE followed by mass spectrometry analyses (including detailed analyses of the methylated region)
- Control of the specific methylation profile by sandwich ELISA
- Stability : at least 1 year at -20°C and at least 2 weeks at 4°C (i.e. no protein degradation)
- Potential scale up to industrial batch sizes: in progress (Potential partnership within an American Association interested in producing industrialized quantity of the antigen).