A new experimental diagnostic test able to quickly distinguish infection from tuberculosis disease

April 1 2011

A potential new experimental diagnostic test able to quickly distinguish individuals with active tuberculosis (TB) from those with latent TB infection has been developed. If the preliminary results of the study will be confirmed in a larger population sample, the new diagnostic system could allow more effective strategies to control the spread of the re-emerging pathology.

The work was performed by a group of scientists from the Catholic University of Rome, the National Institute of Infectious Diseases "L. Spallanzani" of Rome and the University of Sassari, in a study published on the international journal *PLoS One*.

TB is an infection caused by *Mycobacterium tuberculosis*, the bacterium known as Koch's bacillus, named after its discoverer (Robert Koch) in 1882. Following infection with the bacillus, two different scenario may occur: "active disease", clinically evident, and that - if not properly treated - can lead to death and the so called "latent infection", that is asymptomatic and that can last for a lifetime.

Worldwide it is estimated that no less than 2 billion people are infected with the TB bacillus in the latent form, and, luckily, only 5-10% of these infected individuals may develop TB disease. The causes responsible for the manifestation of the disease are still unknown and rapid diagnosis of patients with pulmonary TB is essential to reduce the cure time and to

limit the spread of the infection to the community. Diagnosis of infection with *Mycobacterium tuberculosis* is still performed by the intradermal tuberculin test, developed in the early 20th century, used as a means of screening to determine the spread of infection in the population.

"The tuberculin skin test- explains Delia Goletti, corresponding author of the paper published on *PLoS One* and that together with Dr. Enrico Girardi has coordinated the study at the National Institute of Infectious Diseases 'L. Spallanzani' - has several drawbacks, primarily that is unable to differentiate between infection with environmental mycobacteria (typically not dangerous to humans), vaccination with Bacillus of Calmette et Guerin (BCG) and infection with *M. tuberculosis*. A new assay is being used since ten years, which includes a blood test, based on specific proteins of *Mycobacterium tuberculosis*. The new blood test, called "Interferon-γ release assays (IGRA)", based on the release of interferon-γ in response to *M.* tuberculosis-specific antigens, is able to selectively identify those who have contracted TB infection. "However – continues Delia Goletti - IGRA, as well as the tuberculin test, are not able to distinguish people with latent TB infection compared to those with active TB disease ".

"The results of our study", says Giovanni Delogu, first author of the article, which, together with Prof. Giovanni Fadda has coordinated the research group at the Institute of Microbiology of the Catholic University of Rome - demonstrate that it is possible to distinguish those infected from those with the disease, by simply performing an extra blood test using a protein of the bacillus named HBHA".

"In order for the test to be effective, the HBHA protein must have special features, and to date it has been difficult to obtain large amounts of this protein. – continues Delogu –. Well, our research group has developed an innovative experimental protocol to obtain large amounts

of protein with limited costs, opening the possibility to use this test on a large scale ".

"In this study we have developed an innovative diagnostic algorithm, which consists of a response to the protein HBHA in combination with the IGRA and the results have shown that the response to HBHA associates with latent TB infection. This procedure allows to rapidly identify those who really need the treatment for active TB ", concludes Delia Goletti.

"The response to HBHA can be used as a biomarkers for latent TB infection and then to some extent can be considered as a response of protection to TB. It is important to understand what are the mechanisms triggered by the infection which can cause the appearance or not of the disease", says Stefania Zanetti, professor of Microbiology at the University of Sassari.

"These results – concludes the researchers – open the road to a multicenter study -- "In the future we plan to extend the study to a larger number of patients, giving priority to certain groups where diagnosing active TB can be challenging, such as immunocompromised individuals and children. We also plan to tests the new assay in countries with a high burden of TB".

Provided by Catholic University of Rome

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