News Release

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ATS Press Room: 504-670-6926 (May 15 to 20)

Poster session time: 1:30-4:00 p.m. May 16
Location: CC-Room 260-262 (Second Level), Morial Convention Center

New Technique May Quickly Distinguish between Active and Latent TB

ATS 2010, NEW ORLEANS— An emerging technique designed to quickly distinguish between people with active and dormant tuberculosis may help health professionals diagnose the disease sooner, thereby potentially limiting early exposure to the disease, according to a study conducted by researchers at Duke University Medical Center.

"Current blood tests for tuberculosis are reasonably good at distinguishing between uninfected and infected persons, but cannot tell the whether an infected person has active, and possibly infectious, tuberculosis or has latent infection," said senior author Jason Stout, M.D., M.H.S., assistant professor of medicine at Duke University Medical Center. "Generally a culture is required to tell the difference between latent infection and active tuberculosis, but a culture usually requires weeks to deliver a result. A rapid test that could tell the difference between latent and active tuberculosis would be a major step forward."

The findings will be reported at the ATS 2010 International Conference in New Orleans.

"This pilot study explored whether using patterns in the immune response to tuberculosis could be helpful in improving rapid diagnosis of the disease," Dr. Stout said.

Dr. Stout and colleagues collected whole blood samples from 71 people belonging to one of three groups: those with active tuberculosis, those with latent tuberculosis infection, and those who were not infected with tuberculosis. After exposing the samples to pieces of the tuberculosis bacteria to stimulate an immune response, researchers measured the levels of 25 specific proteins, called cytokines, to determine the presence of a pattern that could allow them to differentiate among the three groups.

“We found that a pattern of two cytokines, called MCP-1 and IL-15, was reasonably good at differentiating between persons sick with TB and persons infected but not sick,” Stout said. “In addition, a third cytokine, called IP-10, looked promising in distinguishing between uninfected persons and infected individuals.”

Stout said that while previous studies identified all three cytokines as possible individual predictors of tuberculosis infection, the usefulness of the combination of MCP-1 and IL-15 was unexpected.

“These findings could lead to earlier diagnosis of active tuberculosis, which could be beneficial for both the sick person and others around her or him who might be spared from infection,” Dr. Stout noted. “There is also the potential for avoiding unnecessary and potentially toxic medications in persons who are not sick with tuberculosis.”

Although the initial results were promising, Dr. Stout noted the sampling for this pilot study was limited, and added that further research would be needed to determine if the results could be replicated in a larger population, “ideally a group of persons suspected of having tuberculosis.”

“Future studies may also help researchers determine whether examining additional cytokines would improve on the accuracy of our results,” he added.

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“Multi-Cytokine Profiles After Tuberculosis Antigen Stimulation: A Search for New Biomarkers for Latent and Active Tuberculosis” (Session A93, Sunday, May 16, 1:30-4:00 p.m., CC-Room 260-262 (Second Level), Morial Convention Center; Abstract 4463)

**Please note that numbers in this release may differ slightly from those in the abstract. Many of these investigations are ongoing; the release represents the most up-to-date data available at press time.*

Multi-cytokine Profiles after Tuberculosis Antigen Stimulation: A Search for New Biomarkers for Latent and Active Tuberculosis

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Introduction. Interferon gamma release assays are powerful new tools for the diagnosis of tuberculosis (TB) infection. However, they do not allow for the rapid differentiation between latent infection and active disease, and may be less useful in children and immunocompromised populations. Examining a profile of multiple cytokines, instead of only interferon gamma, may overcome these limitations.

Methods. We used a Luminex platform to simultaneously evaluate a panel of 25 cytokines/chemokines in whole blood samples following overnight stimulation with mitogen (positive control), saline (negative control), and a mixture of 3 TB antigens from RD1 (ESAT-6, CFP-10, and TB7.7). We defined the response to stimulation as the difference (within an individual patient) in the response to the pooled TB antigens and the negative control. We compared this response among 71 subjects: 12 with active TB, 33 with latent TB, and 26 without evidence of TB infection (negative tuberculin skin test and/or Quantiferon Gold In-Tube®).

Results. Four cytokines had significantly greater response to stimulation in TB-infected persons (active or latent) than in uninfected persons: interferon gamma, IP-10, MCP-1, and IL-15. Of these, two cytokines had significantly greater responses to stimulation among persons with active TB than persons with latent TB: MCP-1 (median response 30,000 pg/mL in active TB vs.11,100 in latent TB, $p=0.002$) and IL-15 (median response in active TB 152 pg/mL vs. 35 pg/mL in latent TB, $p<0.001$). A combination of MCP-1 and IL-15 at cutoffs of >25,000 and 80 pg/mL, respectively, correctly categorized 10/12 active TB infections and 28/32 latent TB infections.

Conclusion. In this pilot study, MCP-1 and IL-15 showed promise as biomarkers to distinguish latent TB infection from active TB disease. Multi-cytokine profiling of the immune response to TB may be useful to develop better clinical tools for TB diagnosis, as well as in understanding the pathophysiology of TB infection.