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# Cystic Fibrosis Research News

**Title:**

SEROLOGICAL BIOMARKERS FOR THE DIAGNOSIS OF *MYCOBACTERIUM ABSCESSUS* INFECTIONS IN CYSTIC FIBROSIS PATIENTS

**Lay Title:**

Serodiagnostic as a complement to bacterial culture in identification of *Mycobacterium abscessus* infections in cystic fibrosis patients

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## What was your research question?

Are there other tests that could improve the diagnosis of non-tuberculous mycobacterial infections by helping interpret the microbiological culture result? Antibodies are produced by the body's immune system to recognize germs that cause infection, including mycobacteria.

Our main objective therefore was to evaluate blood from CF-patients for the presence or absence of several different antibodies against *Mycobacterium abscessus* and compare between people with or without an NTM-positive culture.

## Why is this important?

Culture conditions sometimes are insufficient to detect non-tuberculous mycobacteria (NTM), particularly *M. abscessus*, an emerging infection of concern in CF. The early diagnosis of NTM positive cases not detected by classical culture methods might benefit from the development of a serological assay.

## What did you do?

As part of a diagnostic accuracy study, 173 blood sample from CF-patients were assessed, with 33 patients recording *M. abscessus* positive cultures at the time of blood collection. We also assessed blood from 31 non-CF healthy controls (HC). We used the ELISA method to detect if antibodies against *M. abscessus* were present in the patient's blood. We performed the ELISA test for antibodies against four different parts of *M. abscessus* that the immune system may recognize: two features on the surface of the germ (called Interphase (INP) and a TLR2 positive extract (TLR2eF)) and two parts of a molecule *M. abscessus* used to establish infection (phospholipase C (PLC). We then assessed how good these ELISA results were at accurately identifying which patients were culture positive for NTM.

## What did you find?

Antibodies against TLR2eF and PLC were the most efficient at discriminating between NTM-culture positive and NTM-culture negative CF-patients, with a significant difference between the two groups. Sensitivities (number that were actually NTM-positive) for the TLR2eF and PLC results were 81.2% and 87.9% respectively, and specificities (number that were actually NTM-negative) were 88.9% and 84.8% respectively. We then assessed basing a positive NTM diagnosis on having either the TLR2e or PLC detected by ELISA, and a negative NTM diagnosis, on having both ELISA results as undetected. With this approach for the detection of *M. abscessus*-culture positive CF-patients, we were able to improve sensitivity to 93.9%, while specificity reduced to 80.7%.

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### What does this mean and reasons for caution?

High antibody levels directed against TLR2eF and PLC were obtained in the blood of *M. abscessus*-culture positive CF-patients, allowing us to consider these markers as potential tools in the detection of CF-patients infected with *M. abscessus.* However, several *M. abscessus*-culture positive CF-patients did not have antibodies at the time of blood sampling. This means that as a test, we cannot rule out that someone may have *M. abscessus* when they are antibody negative. On the contrary, although specificity was very high, it was not 100%. It could be that *M. abscessus*-culture negative CF-patients who had these antibodies are either patients with a past NTM infection or more significantly, patients with a current NTM infection that was not detected by culture.

### What's next?

In conclusion, we present here two ELISA assays, which, when combined, provide added value to the diagnostic arsenal we have at our disposal in the mycobacteriology laboratory when considering if a patient has *M. abscessus*. These two ELISA assays are presently being evaluated prospectively in a CF-cohort study called CIMeNT, to determine the prevalence of NTM infections in CF patients in France.

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