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Cystic Fibrosis Research News

Title

Immunoglobulin GM and KM allotypes are associated with antibody responses to *Pseudomonas aeruginosa* antigens in chronically infected cystic fibrosis patients

Lay Title

Genetics of immunity against the *Pseudomonas aeruginosa* bacteria in people with cystic fibrosis

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What was your research question?

We set out to see if genes of the immune system influence the variations among people with CF in the antibody response they make to different bacteria that cause lung infections.

Why is this important?

Antibody responses, in general, are protective against the infecting bacteria, but in chronic infections, such as those caused by *Pseudomonas aeruginosa*, this does not appear to be the case. This study was an attempt to understand why the antibodies people with CF make against infection in the lung do not work well, which will help to discover alternative therapies, such as vaccines and so-called monoclonal antibodies that present an attractive approach for controlling lung infections.

What did you do?

We chose to analyze the variations in the properties of antibodies to some of the more common and important structures on bacteria, termed antigens, that commonly infect people with CF. These variations are known to be distributed among humans within genes that encode the protein parts of antibody molecules. These variations, termed allotypes, could impact the efficiency of antibodies with different variations to provide control of lung infections.

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What did you find?

We found that a person's genetics had a large impact on the levels of the antibodies we studied. We found higher levels of antibodies to bacteria infecting lungs of people with CF associated with number of genes people with CF have. Those with two genes for one variant called KM3 had more antibodies to several of the antigens when compared to those without or with only one copy of this specific variant. Some people with two copies of variants in two different genes had lower antibodies to one of the test antigens.

What does this mean and reasons for caution?

This study showed that gene variations encoding antibody molecules might be important in how a person with CF responds to infectious bacteria in their lungs. This might be important information when designing vaccines and antibodies to be used to prevent or treat CF lung infections. We only studied a few samples, so more studies are needed, but the results will pave the way to help determine how to protect people with CF from lung infections.

What's next?

1. Repeat the study, using sputum and blood samples from a much larger number of people with CF.
2. Investigate whether immunoglobulin genes and antibodies influence the severity of CF lung disease.
3. Investigate how immunoglobulin genes and antibodies cause phagocytosis (engulfment) of bacteria.

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