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Cystic Fibrosis Research News

Title:
Airways glutathione S-transferase omega-1 and its A140D polymorphism are associated with severity of inflammation and respiratory dysfunction in cystic fibrosis.

Lay Title:
Airways glutathione S-transferase omega-1 and inflammation in cystic fibrosis

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What was your research question?
Glutathione S-transferase omega-1 (GSTO1-1) is an enzyme that influences the activity of factors involved in the defence system of the human body (inflammatory response and antioxidant defences). Several genetic variants (polymorphisms) of GSTO1-1 are known. Our aim was to evaluate the possible relations between airways disease in cystic fibrosis (CF) and levels and variants of GSTO1-1.

Why is this important?
The identification of GSTO1-1 variants and their role in the onset of inflammatory response in the airways of people with CF could help to better understand its possible relation with severity of inflammation and breathing problems. This data – together with a better understanding of the role played by GSTO1-1 in the fluid in the lungs – might have both a prognostic as well as a therapeutic significance. Indeed, specific GSTO1-1 inhibitors have been identified and proved capable of modifying the inflammatory response in a range of disease.

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What did you do?

Blood and Sputum samples from a previous study published by our groups were analysed for GSTO1-1 levels and variants. These data were then analysed to find possible correlations with inflammatory markers and lung function .

For comparison, a suitable mouse model of lung inflammation was also used. These mice present with a mutation causing a disease similar to CF in humans, and were prepared with a biomolecular technique that makes the activation of inflammation in the living animal visible. Material from the airways were collected and analysed for GSTO1 detection.

What did you find?

Our data showed that soluble GSTO1-1 can be found in the airways of people with CF and is related to markers of inflammation. A negative correlation was found between GSTO1-1 levels and two lung function parameters. These results were also confirmed in the animal model, where higher levels of GSTO1 were related to the activation of inflammation.

Finally, we observed that one of the major genetic variants of GSTO1-1 was related to lower levels of two anti-inflammatory markers and with unfavourable spirometric parameters in human subjects.

What does this mean and reasons for caution?

Our data suggest that GSTO1-1 and its genetic variants could have a biological and clinical significance in CF. GSTO1-1 could represent an interesting therapeutic target and suitable GSTO1-1 inhibitors could also help deal with such more "pro-inflammatory" GSTO1-1 polymorphisms.

Further studies with larger sample sizes and longer follow-up periods will help to confirm these data.

What's next?

Functions of GSTOs are far from being completely understood, and further studies are required in order to understand the role(s) of GSTO1-1 in the lungs of people with CF.

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