

Cystic Fibrosis Research News

Title:

Intrinsic alterations in peripheral neutrophils from cystic fibrosis newborn piglets

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What was your research question?

We asked whether neutrophils, a type of white blood cells that help in the defence against bacteria, are altered in a pig model of CF. This animal model is considered to be one of the most relevant models to study CF disease.

Why is this important?

Neutrophils are the white blood cells responsible to provide the first response against an invading bacteria or virus (pathogen). They are able to “eat” the pathogen and they release a series of substances (proteases) to the physical surroundings that have the capacity to destroy the bacteria. However, in people with CF, neutrophils seem to be unable to kill the bacteria.

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Instead, neutrophil activity and the release of proteases lead to the destruction of the lungs tissue with severe consequences in people with CF. Therefore, understanding why CF neutrophils fail to carry out their function is important to prevent lung damage during infection in people with CF.

What did you do?

We collected neutrophils from the blood of CF and healthy pigs at birth to study their protein and lipid composition. We used a technique called “Intact cell MALDI-TOF” that allowed us to determine the protein profile of neutrophils. In addition, we evaluated whether neutrophils obtained from CF pigs have the same capacity to kill *Pseudomonas aeruginosa* as those collected from healthy animals.

What did you find?

The most important finding is that CF neutrophils present basic protein alterations already at birth. The data obtained from the “Intact cell MALDI-TOF” analysis also served to develop a mathematical model that can predict whether neutrophils come from a CF or a healthy animal. The major protein differences observed were in the amount of antimicrobial proteins and those related to oxidative stress (a process characterised by an imbalance of free radicals and antioxidants in the body that can lead to cell and tissue damage). However, these differences were not translated into an impairment of CF neutrophil’s ability to kill *Pseudomonas aeruginosa* when compared to those from neutrophils healthy pigs.

What does this mean and reasons for caution?

CF pigs do not present any inflammatory or infectious process at birth that could affect neutrophil maturation. Thus, studying the neutrophil protein composition at this period of life means that our findings are probably related to a direct effect of the CF disease rather than an environmental effect, unravelling new targets for drug development that could improve neutrophil function. However, the data must be taken with caution since our study was performed using blood neutrophils instead of neutrophils collected from the lungs, which can have an important impact on neutrophil maturation.

What’s next?

Further studies are needed to determine whether the observed protein differences have an effect on neutrophil function. In addition, it would be important to study neutrophils isolated from the lungs of CF pigs.



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