

Cystic Fibrosis Research News

Title:

Association of low-density neutrophils with lung function and disease progression in adult cystic fibrosis.

Lay Title:

How the discovery of new white blood cell subtypes can improve our understanding of lung disease progression in adult CF patients?

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What was your research question?

Neutrophils are white blood cells that are called upon to clear the CF lung of invading microbes. Since, neutrophils in CF are not very successful in destroying harmful microbes in the lung, we asked what was different about them compared to neutrophils from healthy individuals.

Why is this important?

Scientists have discovered neutrophil subtypes with unique characteristics in patients with diseases that are characterized by inflammation. These neutrophil subtypes are involved in the disease and are found in a greater proportion in patients with more symptoms. Thus CF patients may have similar neutrophil sub-types since their neutrophils are not able to clear harmful microbes in the lung. For this reason, it is important to determine if CF patients have

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neutrophil subtypes to better understand the disease. Neutrophil subtypes could also help identify patients at risk of having a more severe disease.

What did you do?

We recruited 34 clinically stable, adult CF patients and 35 sex- and age-matched healthy donors. One blood sample of 30ml was harvested from each participant to isolate and purify neutrophil subtypes from the blood to determine their proportion in circulation, their maturity and level of activation. Neutrophil subtypes were compared between CF patients and healthy donors, and we determined if their presence and characteristics were associated with lung disease. Lung disease progression was defined as the variation in lung function over time. The lung function variables used were percentage of predicted forced expiratory volume (ppFEV₁) and frequency of pulmonary exacerbations (PExs). We used statistical analysis to identify associations between neutrophil subtypes and lung disease progression.

What did you find?

We found that adult CF patients have a greater proportion of neutrophil subtypes than healthy individuals in their blood (see ① in the diagram). Neutrophil subtypes are composed of both mature and immature cells that differ in level of expression of cell surface markers (see ② in the diagram). The mature neutrophil subtype is present in a greater proportion in CF patients compared to HD donors. Also, the proportion of the mature neutrophil subtype was higher in CF patients with a greater decline in lung function over time determined with the ppFEV₁. CF patients with frequent PExs during the year before recruitment also had a higher proportion of the mature neutrophil subtype in the circulation compared with patients with no PExs in the last year (see ③ in the diagram).

What does this mean and reasons for caution?

Our findings indicate that, like other diseases in which neutrophils are involved, CF patients have neutrophil sub-types that are more abundant in individuals with severe symptoms. Since neutrophil sub-types do not work properly in other diseases, it is possible that they also malfunction in CF and cause more severe symptoms. Neutrophil sub-types could thus help doctors identify patients with a more aggressive disease. More research is needed to find how neutrophil sub-types are involved in the immune response against infectious microbes in the CF lung and whether they contribute to other aspects of CF.

What's next?

Our next question is if these neutrophil sub-types cause worst symptoms in CF. To answer this question, we will find out whether they are able to eliminate lung microbes efficiently. If not, it will indicate they are a cause of symptoms worsening and lung disease progression in CF.



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Original manuscript citation in PubMed

<https://pubmed.ncbi.nlm.nih.gov/36973151/>

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