

Cystic Fibrosis Research News

Title:

Monocyte Derived Macrophages from CF Pigs Exhibit Increased Inflammatory Responses at Birth

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What was your research question?

We wanted to ask whether macrophages (an important inflammatory blood cell) had a primary defect in cystic fibrosis (CF) that could contribute to disease onset and progression, particularly relating to inflammation. Furthermore, we wanted to know if such an abnormality is present at birth and if it represents a key feature of CF disease.

Why is this important?

The contribution of inflammation to lung damage in CF is not completely understood and previous studies have suggested that macrophages may produce more inflammatory material in CF than in healthy people. If this is true it would represent a target for the development of therapies early in CF disease, before there is established lung damage.

What did you do?

We used blood cells from newborn genetically modified CF pigs (that have no functional CFTR protein) and normal control animals. Using cells (called monocytes) isolated from the peripheral blood (circulating in the body, rather than from the lymphatic system, spleen, liver, or bone marrow) of these animals, we made CF and non-CF macrophages and compared their responses in a number laboratory tests.

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What did you find?

CF and control macrophages looked identical when analysed under a microscope. CFTR protein was present and functional on macrophages from control pigs, but completely absent in CF pigs. This finding suggests that CFTR may have a primary role in macrophage function from early in life. CF pig macrophages had an enhanced inflammatory response to the bacterial stimulus lipopolysaccharide (LPS), suggesting that CF macrophages could promote inflammation as a primary defect in CF.

What does this mean and reasons for caution?

This study shows that there is an abnormality in macrophage function at birth in CF pigs that could contribute to inflammation, and by association, lung damage. We have not performed similar studies using cells of newborn humans. The results of studies from animals do not always completely replicate the human disease. However, the CF pig has been demonstrated to be the best available large animal model of CF to date and develops lung disease with many similarities to people with CF.

What's next?

We would like to confirm these findings in the human disease whilst investigating the potential for targeting this pathway in CF to develop new treatments.

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