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Cystic Fibrosis Research News

Title:

Airway Epithelial Stem Cell Chimerism in Cystic Fibrosis Lung Transplant Recipients

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What was your research question?

We know that lung transplantation (LTx) causes tissue damage and that cells from both the patient and the donor are found in the transplanted lung tissue. We also know that lung tissue stem cells move to areas of severe injury. Since stem cells heal the damaged lung, we wanted to find out if LTx stimulated the stem cells to move?

Why is this important?

Although the survival of people with cystic fibrosis (CF) is the longest among all LTx recipients, most CF LTx recipients develop chronic lung allograft dysfunction (CLAD) – this is when the transplanted lung does not function correctly. This disease may be caused initially by damage to the lung lining and made worse by abnormal repair. If stem cells from the patient move into the transplanted lung, it is possible that they will repair the lung lining and, in the process, generate CF-like tissue. Since CF tissue does not protect the lung from infection, it is possible that that movement of the patient's stem cells and the resulting repair will contribute to the development of CLAD.

What did you do?

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Damage to the lung lining was evaluated in CF LTx recipients using bronchoscopic images (images taken via a tube which is inserted down the throat and into the lungs) and a novel scoring system. Next, stem cells were taken from 10 predetermined sites and we measured how many of these were from the recipient's airways and how many from the transplanted tissue (donor airways). These stem cells were examined for their ability to thrive and for CF Transmembrane Conductance Regulator (CFTR) function. Finally, we used a model to work out if the amount of stem cells from the patient were linked to CLAD.

What did you find?

We found that LTx caused a mild to moderate level of injury to the airway surfaces. Donor and recipient stem cells were found in 91% of sites where the donor and recipient airways had been connected and in 93% of bronchial airways. Mixing of recipient and donor stem cells, which is known as stem cell chimerism, did not alter stem cell function. However, the amount of recipient stem cells was related to the CFTR-dependent ion channel activity and 33% of transplant sites were at risk for abnormal CFTR activity. The amount of recipient stem cells did not correlate with CLAD.

What does this mean and reasons for caution?

We conclude that LTx in people with CF stimulates two-way stem cell migration across the post-surgical connections and that stem cell chimerism was a fundamental component of the cause of disease within the transplanted lung. While our data indicate that stem cell chimerism alters CFTR function and compromises the host defence capability of the transplant airway epithelium, additional analysis is needed to comprehensively test the association between stem cell chimerism and CLAD.

What's next?

Clinical advancements have significantly extended the life expectancy of people with CF. Still, respiratory failure remains the major cause of death and CF is the most frequent indication for LTx in children. A better understanding of why the transplanted lung develops CLAD may lead to better treatments.

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