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Cystic Fibrosis Research News

Title:

Methylomic correlates of autophagy activity in cystic fibrosis

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What was your research question?

Cystic fibrosis (CF) is characterized by a defect in the function of the cells that control infection. These cells are called the immune cells. We wanted to know why these cells fail to control infection.

Why is this important?

This is important because people with cystic fibrosis (CF) become infected with bacteria that do not infect healthy individuals. Unfortunately, most of these bacteria cannot be killed by usual treatment and many people with CF cannot clear the infection and become extremely sick. So, we have to find ways to improve the function of the immune cells in people with CF to help them combat infection.

What did you do?

We studied a function in immune cells called "autophagy" which means self-eating. Autophagy can digest bad proteins and produce nutrients for the cell during starvation. Autophagy can also digest the bacteria and stop the infection. We found that autophagy is not working in immune cells from people with CF or from a mouse model that mimics CF

disease. We measured if all the factors needed for autophagy are produced at good levels in the CF immune cells. We found that several of these autophagy proteins are produced at very low levels. In this study, we used a very novel technique called RRBS (reduced representation bisulfite sequencing) not previously used in CF.

What did you find?

Using RRBS, we found that these autophagy proteins are not produced at the needed level because the machinery that produces these proteins is occupied with a blocking molecule. This blocking molecule is called methyl group. If the methyl group is removed, the machinery will be able to produce the needed autophagy proteins. Fortunately, there is a compound derived from green tea called EGCG that is known to remove methyl groups from the machineries that make proteins. It has been used in other diseases like diabetes and cancer. We used EGCG on live mice and we found that it improves autophagy and improves the clearance of bacteria. EGCG removed the methyl group from the machinery that makes the autophagy proteins and increased their production.

What does this mean and reasons for caution?

This study is important because it explains why the CF immune cells fail to control infection. It also shows that EGCG can improve their functions and make them able to digest bacteria by autophagy. EGCG is extracted from green tea and has minimal side effects. It has been used in other diseases characterized by weak autophagy activity.

What's next?

This finding will encourage others to find ways to improve autophagy in CF immune cells in order to improve bacterial clearance.

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