Advancing Cystic Fibrosis Treatment through Synthetic Carriers for Anion Transport

Cystic fibrosis (CF) is a life-threatening disease that affects thousands of people worldwide. When the causative gene of CF was identified almost three decades ago, it generated hope for an imminent cure. CF is a genetic disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that encodes the CFTR protein. This protein acts as a channel, transporting molecules with a negative electrical charge (called anions), which have a direct influence on the control of water transport and mucus formation. In individuals with CF, the transport of anions is impaired, leading to mucus buildup in the lungs and other organs. Although some medicines targeting CFTR abnormalities have been developed, their effectiveness has been limited until now.

In this study, we restored anion transport in CF cells by introducing artificial anion carriers (anionophores) into patients' lung cells. These anionophores replace the faulty CFTR protein, relieving CF symptoms. We designed and tested 22 different anionophores, and found that three of them exhibited anion transport activity similar to or greater than that of a previously studied anionophore. We found that all four compounds were capable of transporting anions in and out of lab-cultured lung cells. Moreover, when paired with two clinically approved drugs for CF, lumacaftor and ivacaftor, these compounds enhanced anion transport in cells with the F508 deletion (which is the most prevalent CFTR mutation associated with CF). Further, these compounds exhibit low levels of toxicity.

Thus, we concluded that synthetic anionophores can be used in CF therapy, either alone or in conjunction with other treatments. We are hopeful that with further advancements, these synthetic carriers will lead to successful and widespread therapy for CF.

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