Science Translational Medicine

RESEARCH ARTICLE | LUNG DISEASE

A PI3Kγ mimetic peptide triggers CFTR gating, bronchodilation, and reduced inflammation in obstructive airway diseases

ALESSANDRA GHIGO, ALESSANDRA MURABITO, VALENTINA SALA, ANNA RITA PISANO, SERENA BERTOLINI, AMBRA GIANOTTI, EMANUELA CACI, ALESSIO MONTRESOR, AISWARYA PREMCHANDAR, [...] EMILIO HIRSCH +37 authors Authors Info & Affiliations

SCIENCE TRANSLATIONAL MEDICINE · 30 Mar 2022 · Vol 14, Issue 638 · DOI: 10.1126/scitranslmed.abl6328

GET ACCESS

PI3K-ing a mimetic

Increasing cyclic adenosine monophosphate (cAMP) in the airways of patients with obstructive lung diseases can reduce airway inflammation and constriction. However, current therapies can induce treatment-limiting systemic side effects. Here, Ghigo and colleagues found that phosphoinositide 3-kinase γ (PI3Kγ) negatively regulated the β_2-adrenergic receptor signaling pathway to decrease cAMP. They created a PI3Kγ mimetic peptide that increased local cAMP concentrations and, when administered intratracheally in a mouse model of asthma, induced airway relaxation and reduced neutrophil infiltration. Further, in airway epithelial cells from patients with cystic fibrosis, it triggered gating of the cystic fibrosis transmembrane conductance regulator (CFTR) channel and enhanced the effects of CFTR modulators, suggesting that the PI3Kγ mimetic peptide may be used to treat obstructive lung diseases in humans.