Cystic fibrosis transmembrane conductance regulator in COPD: a role in respiratory epithelium and beyond

Marcus A. Mall[1,2,3], Gerard J. Criner[4], Marc Miravitlles[5], Steven M. Rowe[6], Claus F. Vogelmeier[7], David J. Rowlands[8], Matthias Schoenberger[9] and Pablo Altman[10]

[1]Department of Pediatric Respiratory Medicine, Immunology and Critical Care Medicine, Charité–Universitätsmedizin Berlin, Berlin, Germany. [2]Berlin Institute of Health, Berlin, Germany. [3]German Center for Lung Research, associated partner, Berlin, Germany. [4]Department of Thoracic Medicine and Surgery, Lewis Katz School of Medicine at Temple University, Philadelphia, PA, USA. [5]Pneumology Department Hospital Universitari Vall d'Hebron, Vall d'Hebron Institut de Recerca (VHIR), Vall d'Hebron Hospital Campus, CIBER de Enfermedades Respiratorias (CIBERES), Barcelona, Spain. [6]Univeristy of Alabama at Birmingham, Birmingham, AL, USA. [7]Department of Medicine, Pulmonary and Critical Care Medicine, University of Marburg, member of the German Center for Lung Research (DZL), Marburg, Germany. [8]Novartis Institutes for Biomedical Research, Cambridge, MA, USA. [9]Novartis Pharma AG, Basel, Switzerland. [10]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA.

Corresponding author: Marcus A. Mall (marcus.mall@charite.de)

Shareable abstract (@ERSpublications)
Acquired CFTR dysfunction may increase COPD pathogenesis through CFTR impairment across multiple cell types, including epithelial, immune and structural cells. CFTR potentiation may lead to an overall improvement in lung health in patients with COPD. http://bit.ly/3VlR7S5

Cite this article as: Mall MA, Criner GJ, Miravitlles M, *et al*. Cystic fibrosis transmembrane conductance regulator in COPD: a role in respiratory epithelium and beyond. *Eur Respir J* 2023; 61: 2201307 [DOI: 10.1183/13993003.01307-2022].

This single-page version can be shared freely online.

Copyright ©The authors 2023.

This version is distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 4.0. For commercial reproduction rights and permissions contact permissions@ersnet.org

Received: 28 June 2022
Accepted: 17 Nov 2022

Abstract

The cystic fibrosis transmembrane conductance regulator (CFTR) is a crucial ion channel for transport of chloride and bicarbonate anions. Functional roles of CFTR have been identified in a broad range of cell types including epithelial, endothelial, immune and structural cells. While CFTR has been investigated largely in the context of inborn dysfunction in cystic fibrosis, recent evidence shows that CFTR is also affected by acquired dysfunction in COPD. In patients with COPD and smokers, CFTR impairment has been demonstrated in the upper and lower airways, sweat glands and intestines, suggesting both pulmonary and systemic defects. Cigarette smoke, a key factor in COPD development, is the major cause of acquired CFTR dysfunction. Inflammation, bacterial byproducts and reactive oxygen species can further impair CFTR expression and function. CFTR dysfunction could contribute directly to disease manifestation and progression of COPD including disturbed airway surface liquid homeostasis, airway mucus obstruction, pathogen colonisation and inflammation. Mucus plugging and neutrophilic inflammation contribute to tissue destruction, development of dysfunction at the level of the small airways and COPD progression. Acquired CFTR dysfunction in extrapulmonary organs could add to common comorbidities and the disease burden. This review explores how CFTR dysfunction may be acquired and its potential effects on patients with COPD, particularly those with chronic bronchitis. The development of CFTR potentiators and the probable benefits of CFTR potentiation to improve tissue homeostasis, reduce inflammation, improve host defence and potentially reduce remodelling in the lungs will be discussed.