Cystic Fibrosis Translational Research CENTRE de Recherche Translationnelle sur la Fibrose Kystique

McGill School of Biomedical Sciences | École des sciences biomédicales

CFTRc Seminar Series

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CFTR independent pathways that regulate airway surface liquid pH

Airway surface liquid (ASL) pH homeostasis is disrupted in CF due to faulty CFTR, which compromises innate defence mechanisms, predisposing to pulmonary failure. Therefore, restoring ASL pH homeostasis is a potential therapy for people with CF, particularly for those who cannot benefit from current highly effective modulator therapy (HEMT). However, we lack a comprehensive understanding of the complex mechanisms underlying ASL pH regulation, particularly in the absence of a functional CFTR. Possible alternative targets that impact ASL pH include; Na/H exchangers, proton-ATPase, SLC26A ion transporters and TMEM16A, a calcium-activated chloride channel. This talk will describe our recent work investigating the role of TMEM16A and SLC26A family members (SLC26A4 and SLC26A9) in acid-base homeostasis. To do this we employed CRISPR-Cas9 to knock-out the transporters in primary airway epithelial basal cells lacking CFTR, and then measured dynamic changes in ASL pH under thin-film conditions in fully differentiated airway cultures, under normal and inflammatory conditions. Our results show that TMEM16A and SLC26A4 both play complex roles in ASL pH homeostasis, but SLC26A9 does not, in cells lacking CFTR. Overall, this suggests that both TMEM16A and SLC26A4 could be important alternative targets for ASL pH therapy in CF, particularly for those people who do not produce any functional CFTR.

Date: **Tuesday, May 23, 2023**

Time: **11:00 a.m.**

Online via Zoom:

https://mcgill.zoom.us/j/84876902038?pwd=NmpyUXlrVUtWdHhoNlpvVHErZ1RxZz09

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