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[ATS] CFTR Potentiator Ivacaftor, A Novel Mucus Clearance Therapy In COPD

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CFTR PotentiatorIvacaftor, a Novel Mucus Clearance Therapy in COPD

COPD patients exhibit diminished Cystic Fibrosis Transmembrane Conductance Regulator **(CFTR)**-dependent ion transport resembling that of cystic fibrosis (CF), potentially causing mucus obstruction.
In healthy airways, CFTR conducts anions across the epithelium to drive airway hydration, mucus maturation, and mucociliary clearance (MCC).

We have **previously shown that the CFTR potentiatorivacaftor (VX-770) can improve CFTR anion transport in smoke-exposed epithelia**, potentially ameliorating MCC in COPD.

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METHODS

Effects of ivacaftor on mucociliary properties were evaluated with micro-optical coherence tomography (µOCT) imaging in primary human **bronchial epithelial (HBE)** cells **exposed** to 2 % cigarette smoke extract (CSE), or human bronchial tissues exposed to whole cigarette smoke (WCS) from one 3R4F cigarette for 10 minutes, **and compared** to DMSO (Vehicle) or air **controls**.
Tomography (µOCT) simultaneously quantified airway surface liquid (ASL) depth, ciliary beat frequency (CBF), and mucociliary transport (MCT). Changes in mucus viscosity were determined using time of fluorescent recovery after photobleaching (FRAP).

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RESULTS

In HBE cells, **cigarette smoke reduced ASL** height by 36 % (Veh 13.3 ± 0.7, CSE 8.4 ± 0.6 µm), **CBF** by 15 % (Veh 5.9 ± 0.2, CSE 5.0 ± 0.1 Hz), and **MCT** by 98 % (Veh 0.25 ± 0.03, CSE 0.004 ± 0.002 mm/min**). Ivacaftor rescued these smoke-induced effects** on ASL (18.8 ± 1.3 µm, $p < 0.001$), CBF (6.62 ± 0.2 Hz, $p < 0.001$), and MCT (0.25 ± 0.03 mm/min, $p < 0.001$).

FRAP indicated **ivacaftor reduced mucus viscosity in airway tissues from non-smokers and healthy smokers** by 56 % (Veh 14.9 ± 0.3, ivacaftor 6.4 ± 0.6 s, $p < 0.0001$).

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CONCLUSIONS:

CFTR activation by **ivacaftor overcomes cigarette smoke-induced mucus clearance abnormalities**.

Ivacaftor conferred marked improvements in MCT in smoke-exposed bronchial tissue by reducing mucus viscosity, indicating its potential as a novel COPD therapy.

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