Airway inflammation plays a key role in the pathogenesis of cystic fibrosis (CF) and results from a combination of repeated bacterial lung infection and an exaggerated host response. The aim of this study was to assess exhaled NO and exhaled breath condensate (EBC) pH to study airway inflammation in CF patients and controls. Samples were collected from 32 CF patients, of which 9 were chronically colonized with Pseudomonas aeruginosa (PA) and 21 healthy controls (age 6–23 yrs). NO was measured with a NIOX Mino (Aerocrine). EBC was collected using a RTube (Respiratory Research, 15 min tidal breathing). pH was measured without deaeration. NO was significantly lower in CF compared to controls (median: 8 (interquartile range (IQR) 6−10) versus 10 (IQR 9–16) ppb respectively; p=0.003). There was a significant difference between CF with and without PA (6 (IQR 3−7) vs 8 (IQR 7–10) ppb respectively; p=0.003). Heavy (p<0.01) and taller (p<0.01) children had higher NO values. EBC pH was lower in CF patients than in controls (median: 5.38 (IQR 5.06–5.65) vs 5.70 (IQR 5.25–6.07) respectively), but this was not significant. Females had lower EBC pH than males (p=0.03). Collected volume EBC was significantly higher in controls (median 1.7 ml; IQR 1.5–2.0) compared to CF patients (1.4 ml; IQR 1.0–1.6; p=0.04). Between the CF patients, the volume was higher in CF with PA (1.6 ml; IQR 1.3–2.0) vs CF without PA (1.2 ml; IQR 0.9–1.6; p=0.03). Older (p<0.01), heavier (p=0.04) and taller (p=0.01) children collected more EBC. In conclusion, significant differences were observed for NO between CF and healthy controls and CF with and without PA. EBC pH was lower in CF, but this was not significant. Supported by a grant of Belgian CF association.

**Critical role for cytosolic phospholipase A2 in bronchial mucus hyper-secretion in CFTR−/− mice**

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Cystic fibrosis (CF) is caused by mutations in the gene encoding CF transmembrane conductance regulator (CFTR). Mucus, a complex structure mainly composed of water, ions and mucins, plays an important role in host defence against invading pathogens. However, the mechanisms linking CFTR alteration to mucus overproduction, observed in CF, remain unclear. Cytosolic phospholipase A2 (cPLA2) in an enzyme which cleaves membrane phospholipids of mammalian cells leading to a selective release of arachidonic acid (AA). We report here enhanced mucus production associated to increased cPLA2 activity in lung of CFTR−/− compared to wild-type mice. This was accompanied by an increased expression of a particular mucin, Muc5ac. These processes were exacerbated by intranasal instillation of Pseudomonas aeruginosa LPS and accompanied by increased concentrations of AA in broncho-alveolar lavages fluids. Mucus production was enhanced by intranasal AA instillation. Disruption of the gene encoding cPLA2 or treating CFTR−/− mice with a cPLA2 inhibitor abrogated mucus production and Muc5ac expression. Finally, enhanced cPLA2 activity and AA concentrations were evidenced in bronchial explants of CF patients. We conclude that CFTR alteration in CF lungs induces an abnormal cPLA2 activation, which in turn enhances mucus production via AA. We propose a potential therapeutic role for cPLA2 inhibitors in reducing mucus accumulation in CF. The signalling pathways involved in the induction of Muc5ac expression in epithelial cells are under investigation.

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**Sphingomyelinase and ceramidase activities in tissues of delta-F508 CFTR mice**

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**Background:** Sphingolipid signalling may differ between individuals with CF and healthy controls. The response to bacterial inflammation is different, and uptake and inactivation of sphingosine-1-phosphate, an intracellular pro-inflammatory mediator, is reduced in CF cells. It may therefore continue to act on G-protein coupled receptors in the plasma membrane. (Boujoud et al, J Biol Chem 2001). Furthermore, ceramide originating from basolateral sphingomyelin hinders augmentation of CFTR-mediated anion conductance across the apical membrane, resulting in reduction of transepithelial airway anion secretion (Bo et al, BBRC 2004)

** Aim of study:** To determine if there is a difference in the levels of alkaline, neutral or acid sphingomyelinase (SMase), or in the levels of neutral or acid ceramidase, in the intestinal or bronchial mucosa and some other tissues, between wildtype (+/+), homozygous (−/−) and heterozygous (−/+)- delta-F508 CFTR mice.

**Methods:** Enzyme activities (Duan and Nilsson Meth Enzymol 2000) were determined in intestine (and content) divided into four regions, liver, lungs, kidney and spleen from deltaF508-CFTR mice (−/−) and controls (+/−, +/+).

**Results:** There was an increased amount of neutral ceramidase in spleens from deltaF508-CFTR mice (−/−) in comparison to control mice (p=0.0278). No other significant differences were seen.

**Conclusion:** Delta-F508 mutation did not influence the levels of alkaline SMase and neutral ceramidases acting as ectoenzymes, or the levels of intracellular SMases and ceramidases, which may all generate bioactive sphingolipid metabolites in intestine and lungs. The implications of the increased level of neutral ceramidase in spleen are not known.