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Airway surface liquid composition in mice

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Keywords

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Introduction

One hypothesis linking mutations in CFTR with lung disease suggests that the airway surface liquid in the lung of CF patients is altered due to the defective (CFTR) epithelial chloride channel. This altered liquid has been proposed to effect the antibacterial properties of the lung, or the viscosity of the mucus, leading to the perpetual lung infections which ultimately limit survival in most CF patients. The ionic composition of the airway surface liquid was measured in different inbred strains of mice and in knockout mice lacking functional CFTR (CF mice).

Comments

The airway surface liquid (ASL) of cystic fibrosis (CF) patients is presumed to be altered due to a defective epithelial chloride channel, encoded by CFTR. If verified, this could be a hypothesis linking the defective chloride channel to lung disease. It has been demonstrated *in vitro* that the antibacterial functions of the lung are compromised by changes in the ionic composition of the ASL. CF mouse models will be useful to investigate the hypothesis that the ASL is altered in CF patients, and an initial study is reported here. The main conclusion of the work is that adult CF and normal littermate mice did not differ in the ionic composition of their ASL. Similar results have been shown *in vitro*, using tracheal epithelial cells from a different CF mouse model. One potential limitation of the study is that the ascertainment of ASL suffers from sampling bias, as this liquid is actively regulated by epithelial cells which may respond to the collection. Although the technique used here has been used with success by these authors in rats, it is known to be subject to plasma contamination through epithelial injury. The authors addressed this by histologically confirming the trachea to be normal after the procedure. If confirmed in a larger data set (only five CF mice were evaluated) these results may demonstrate that CF mice are able to maintain normal ionic composition of the ASL without functional CFTR.

Methods

SL sampling: anaesthetized mice (C57BL/6, A/J, BALB/c, B6-Cfr UNC^{-/-}) were tracheotomized and a sampling capillary (PE-10 tubing) was inserted into the trachea so that its end lay in contact with the epithelium at the base of the trachea

The sample was collected for 30 min (volume collected = 100/200 nL) and analysed by capillary electrophoresis

Submucosal gland distribution was assessed through image analysis of histological sections

Results

The concentrations of sodium and chloride ions were significantly lower in the ASL than they were in plasma, as in other studies including ones using humans. The ASL ionic composition in five B6 CF mice was similar to their littermate controls (n = 25). Inbred mouse strain differences in the amount of ASL that could be harvested were reported, and attributed to differences in submucosal gland distribution among the strains.

Discussion

The authors reiterate that ASL collection in this small animal is challenging, and despite imperfect data, the results agree with the studies in other species. The principal finding presented is that murine ASL has a lower salinity than plasma. In a limited study, the ASL of CF mice was found to not differ from that of wild-type littermates. The ionic concentration of potassium in the ASL of mice differs from previous reports in rats, which is attributed to species or sample collection differences.

Additional information

References

1. Cowley EA, Govindaraju K, Guilbault C, Radzioch D, Eidelman DH: Airway surface liquid composition in mice. *Am J Physiol.* 2000, 278: L1213-L1220.