In vitro bioelectric properties of bronchial epithelium from transplanted lungs in recipients with cystic fibrosis

Victor T Tsang, Eric W F W Alton, Margaret E Hodson, Magdi Yacoub

Abstract

Background—Bronchial epithelial function after heart-lung transplantation (HLT) for cystic fibrosis (CF) may be affected by the original disease as well as other factors such as prolonged organ ischaemic time, the interruption of bronchial arterial and lymphatic supply, infection, rejection, and cyclosporin. In vitro measurement of the bioelectric properties of the bronchial mucosal lining may be an effective means of characterising the mucosal function of the lung allografts in response to pharmacological agents.

Methods—Bronchial mucosal tissues from explanted native lungs of CF and non-CF patients at transplantation were used to assess the possible application of a mini-Ussing chamber. With this technique, the bioelectric responses of bronchial mucosal biopsies from six patients with CF, one patient with congenital heart disease, four with primary pulmonary hypertension, and one with emphysema, all after HLT, were studied. The bioelectric and pharmacological responses of biopsies of bronchial mucosa from patients after HLT were compared with biopsies from non-CF non-HLT subjects.

Results—The altered bioelectric properties of CF tissues could be detected by the mini-Ussing chamber technique. The basal bioelectric values and the responses to amiloride and isoprenaline in CF patients were not different from those in non-CF patients two years after HLT. No significant difference in the basal bioelectric properties and responses to amiloride and isoprenaline was found between HLT recipients and non-CF non-HLT subjects.

Conclusions—The mini-Ussing chamber is an effective means of characterising the typical CF bioelectric defect which was not found in the transplanted lungs of CF patients up to two years after HLT. Furthermore, values were unaltered in comparison with non-transplanted lungs, suggesting that bronchial epithelial function is maintained after HLT.

Cystic fibrosis (CF) is an inherited disease affecting primarily the epithelium of the airways, gastrointestinal tract, and sweat glands. The underlying defect in CF relates to abnormalities of ion transport across these epithelia which, in the airways, probably contributes to the thickened mucus and recurrent chest infections typical of patients with CF. The principal defect in CF relates to a low chloride permeability in all affected tissues. Single channel studies have shown that regulation of apically located chloride channels in airway epithelia are defective. Thus in normal cells, activation of the protein kinase A or C second messenger pathways results in an increase in the probability of channel opening. By contrast, phosphorylation via these pathways fails to activate chloride channels from CF airway cells. Isoprenaline, a β adrenergic agonist, activates adenylate cyclase, raises the concentration of cyclic AMP, and induces chloride secretion in normal tissue; in tissue from patients with CF this response is noticeably reduced, probably due to defective phosphorylation of the channel by protein kinase A.

In both airway and gastrointestinal epithelia from patients with CF there is an increased rate of sodium absorption, which in the first probably accounts for the abnormally high (more negative) potential difference across the respiratory epithelium. Thus the application of amiloride, a sodium channel blocker, produces a significantly lower potential difference (less negative) in CF compared with non-CF airways.

Heart-lung transplantation (HLT) has been successfully performed for patients with CF who have end stage respiratory failure. In patients with CF, the potential difference of the transplanted airways measured in vivo did not differ from those in non-CF non-HLT patients up to two years after transplantation, although the nasal potential difference in the patients with CF remained abnormal. The lower airway potential difference profile in both CF and non-CF patients after HLT was altered, however, compared with those of non-CF non-HLT patients. The function of the bronchial epithelium after HLT may be adversely affected by various factors. These include the interruption of bronchial arterial and lymphatic supply, rejection, infective episodes,
and possibly cyclosporin. It has recently been shown that cyclosporin may affect intestinal epithelial permeability in rats.16

The routine assessment of transbronchial biopsies from HLT recipients provides the opportunity for more detailed in vitro characterisation of the bioelectric responses of the bronchial epithelium. To allow for the small tissue samples obtained from bronchoscopic biopsies, mini-Ussing chambers were used to study bioelectric responses in vitro. Jejunal biopsies taken from patients with and without CF and mounted in such chambers with 2 mm diameter apertures are clearly distinguishable on the basis of their bioelectric responses to pharmacological interventions.17

A similar technique has also been used to show the failure of chloride secretion in biopsies of rectal mucosa from patients with CF.1819 We have, therefore, assessed the feasibility of studying bronchoscopically obtained biopsies mounted in these mini-Ussing chambers. We have also studied the effect of HLT on the in vitro pharmacological responses of pulmonary tissue up to two years after transplantation.

Patients and methods

PATIENTS

CF non-HLT patients

Explanted native lungs obtained at transplantation from five patients with CF (one male and four female) with a median age of 29 (range 8–39) years were studied to provide baseline CF bioelectric parameters.

Non-CF non-HLT “controls”

Unused lungs from three donors (age range 20–26 years; one man and two women) and explanted lungs obtained at transplantation from six non-CF patients (age range 21–32 years; two men and four women) were studied as an additional control group for effects of the transplant operation and immunosuppressive treatment. The diagnoses in the six non-CF patients included Eisenmenger’s syndrome (one), primary pulmonary hypertension (one), emphysema (two), bronchiectasis (one), and fibrosing alveolitis (one).

CF HLT patients

Five HLT recipients with CF (two men and three women) with a median age of 30 (range 25–39) years were studied two to 24 months after HLT (table 1). The indications for bronchoscopy, transbronchial biopsy and bronchoalveolar lavage were regular review in two patients, possible allograft rejection in two, and infection in one.

Non-CF HLT patients

Six non-CF HLT recipients (two men and four women) with a median age of 20 (range 17–46 years) were studied (table 1). The diagnoses in these patients included Eisenmenger’s syndrome (one), primary pulmonary hypertension (four), and emphysema (one). The indications for transbronchial biopsy and bronchoalveolar lavage were regular bronchoscopic review in three patients and reduced lung function with possible rejection in three. Bronchial mucosal biopsies were taken three to 12 months after HLT.

Treatment at the time of bronchoscopy in both groups of HLT patients included cyclosporin, azathioprine, prednisolone, aspirin, ranitidine, frusemide, antibiotics, and in the case of patients with CF, pancreatic enzyme and vitamin supplements.

BRONCHOSCOPIC PROCEDURE AND SITES OF BRONCHIAL MUCOSAL BIOPSY

Ethics committee approval was obtained for all procedures. Biopsies of bronchial mucosa were obtained from HLT recipients at the time of transbronchial biopsy and bronchoalveolar lavage. Under general anaesthesia, rigid bronchoscopy was undertaken and one biopsy was taken from the main carina with a cup shaped rigid bronchoscopic biopsy forceps. Tissues were immediately placed in cold oxygenated Krebs-Henseleit solution, composition (mM/l): Na+ 145-0; K+ 5-9;

Table 1  Details of HLT patients (CF and non-CF) undergoing bronchoscopy

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age (y)</th>
<th>Time from HLT (months)</th>
<th>Indications</th>
<th>BAL/TBB findings</th>
<th>FEV1/FVC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>25 M</td>
<td>6</td>
<td>Follow up</td>
<td>Negative</td>
<td>2-5/3-4</td>
</tr>
<tr>
<td>2</td>
<td>37 M</td>
<td>2</td>
<td>Pyrexial; rejection</td>
<td>Negative</td>
<td>1-7/2-1</td>
</tr>
<tr>
<td>3</td>
<td>39 F</td>
<td>6</td>
<td>Follow up</td>
<td>Positive</td>
<td>3-4/3-5</td>
</tr>
<tr>
<td>4</td>
<td>26 M</td>
<td>24</td>
<td>Productive cough</td>
<td>Negative</td>
<td>3-2/3-4</td>
</tr>
<tr>
<td>5</td>
<td>30 F</td>
<td>12</td>
<td>Pyrexial; rejection</td>
<td>Negative</td>
<td>2-2/2-6</td>
</tr>
<tr>
<td>Non-CF:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>18 F</td>
<td>12</td>
<td>Reduced lung function</td>
<td>Rejection</td>
<td>0-8/0-9</td>
</tr>
<tr>
<td>2</td>
<td>46 M</td>
<td>3</td>
<td>Rejection?</td>
<td>Negative</td>
<td>1-0/1-9</td>
</tr>
<tr>
<td>3</td>
<td>17 M</td>
<td>6</td>
<td>Follow up</td>
<td>Negative</td>
<td>2-1/2-2</td>
</tr>
<tr>
<td>4</td>
<td>30 F</td>
<td>9</td>
<td>Reduced lung function</td>
<td>Rejection</td>
<td>1-4/2-7</td>
</tr>
<tr>
<td>5</td>
<td>17 F</td>
<td>7</td>
<td>Follow up</td>
<td>Negative</td>
<td>3-1/3-2</td>
</tr>
<tr>
<td>6</td>
<td>21 M</td>
<td>12</td>
<td>Follow up</td>
<td>Negative</td>
<td>2-2/2-6</td>
</tr>
</tbody>
</table>

BAL—bronchoalveolar lavage; TBB—transbronchial biopsy; FEV1—forced expiratory volume in one second; FVC—forced vital capacity.
Ca\(^{2+}\) 2·5; Mg\(^{2+}\) 1·2; Cl\(^{-}\) 126·0; HCO\(_3\)\(^{-}\) 26·0; PO\(_4^{3-}\), 1·2; glucose 5·0), and transported to the laboratory on ice.

The intact airways from explanted lungs (CF and non-CF) obtained at transplantation and unused donor lungs were transported to the laboratory as described. Biopsy samples were taken in two ways. Firstly, a rigid bronchoscopic biopsy forceps was used and one biopsy was taken from the main carina under direct vision (termed 3 mm biopsy for mounting in mini-Ussing chambers of aperture diameter 2 mm). This preparation, in practice, is similar to the tissue available from HLT patients at follow up bronchoscopy. Secondly, the airways were opened longitudinally and roughly 3 mm and 5 mm diameter samples were removed by fine dissection for mounting in 2 mm and 4 mm chambers, respectively (termed 3 mm and 5 mm sheets).

**MEASUREMENT OF BRONCHIAL MUCOSAL BIOELECTRIC PROPERTIES**

Tissue samples were mounted in the mini-Ussing chambers under open circuit conditions. Tissues were bathed on each side with Kreb’s solution (5 ml), pH 7·4 at 37°C, and gassed with 95% oxygen and 5% carbon dioxide. Potential difference was measured with 1 M KCl 2% agar bridges placed within 0·5 mm of either side of the tissue and connected via calomel half cells (Russell pH Ltd, Fife, Scotland) to a differential input electrometer (fig). Tissue resistance was calculated from the change in potential difference induced by passage of 10 μA of current through Ag/AgCl wires and 0·9% NaCl 2% agar bridges. Fluid resistance was similarly measured before tissue mounting and appropriate adjustments were made to the measured resistance. Equivalent short circuit current (Isc\(_{eq}\)) was then calculated from Ohm’s law.\(^{17-19}\)

Tissue samples with resistance less than 10 ohm/cm\(^2\) were discarded due to poor bioelectric responses. The number of tissue samples then available for study comprised: from the five CF non-HLT patients, 16 of 5 mm sheets (mean three, range one to six per lung), 15 of 3 mm sheets (mean three, range two to five per lung), and five of 3 mm biopsies from five lungs. From the non-CF non-HLT controls, the specimens included nine of 5 mm sheets (mean one, range one to two per lung), 13 of 3 mm sheets (mean one, range one to four per lung), and six of 3 mm biopsies from six “control” lungs. From the HLT patients (five CF and six non-CF), only one bronchial mucosal biopsy was taken from each patient at the time of bronchoscopic evaluation. After bioelectric studies, data obtained from all specimens of any one patient were averaged (n values are the number of patients studied).

**EFFECTS OF APPLICATION OF PHARMACOLOGICAL AGENTS ON TISSUE BIOELECTRIC PROPERTIES**

After stabilisation of the potential difference of the tissue (defined as a change of less than 10% over 10 minutes), two measurements of basal values were taken with a five minute interval. Amiloride (10 μM) was added to the mucosal solution and readings were taken at one minute intervals for a further 10 minutes. Isoprenaline (10 μM) was then added to the serosal chamber and readings were taken at five minute intervals for a further 45 minutes. The bioelectric response was calculated as the difference between the maximal potential difference generated with an agent, and the stable potential difference before its addition. Amiloride was a gift from Merck, Sharpe, and Dohme. All other chemicals were purchased from Sigma Chemical Co, UK and BDH Ltd, UK, and were of AnalR grade or the best available.

**OTHER INVESTIGATIONS**

Bronchoalveolar lavage was performed by wedging the tip of the fibroptic bronchoscope in one of the subsegmental bronchi of the lower lobe. Up to 160 ml of warm sterile sodium bicarbonate buffered normal saline were injected in aliquots of 40 ml with sequential aspirations. About 60 to 80 ml of lavage fluid were recovered. Samples were placed in sterile siliconised bottles and processed immediately for cellular profile of the lavage fluid and microbiology, including

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*Schematic representation of the mini-Ussing chamber technique (modified from Hardcastle et al)*.

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Table 2 Bioelectric properties of biopsies of bronchial mucosa from non-CF non-HLT and CF non-HLT bronchial tissues: effects of mucosal amiloride and serosal isoprenaline

<table>
<thead>
<tr>
<th></th>
<th>Non-CF non-HLT</th>
<th>CF non-HLT</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isc (µA/cm²)</td>
<td>15.3 (3.9)</td>
<td>13.7 (3.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Potential difference (mV)</td>
<td>0.5 (0.1)</td>
<td>0.4 (0.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Amiloride (10 µM):</td>
<td>-53.1% (10.3)</td>
<td>-66.4% (8.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Resistance (ohms/cm²):</td>
<td>-1.6% (1.8)</td>
<td>-2.3% (1.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Isoprenaline (10 µM):</td>
<td>48.0% (7.1)</td>
<td>1.0% (1.3)</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Resistance (ohms/cm²):</td>
<td>0.9% (3.3)</td>
<td>0.6% (0.9)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Basal properties are expressed as means (SE) and bioelectric responses as mean % changes (SE).

Isceq, equivalent short circuit current calculated from Ohm's law, indirectly by determining resistance and potential difference; CF—cystic fibrosis; HLT—heart-lung transplantation.

Table 3 Bioelectric properties of biopsies of bronchial mucosa from non-CF HLT and CF HLT patients: effects of mucosal amiloride and serosal isoprenaline

<table>
<thead>
<tr>
<th></th>
<th>Non-CF HLT</th>
<th>CF HLT</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isceq (µA/cm²)</td>
<td>11.2 (1.6)</td>
<td>7.3 (1.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Potential difference (mV)</td>
<td>0.26 (0.06)</td>
<td>0.22 (0.06)</td>
<td>NS</td>
</tr>
<tr>
<td>Resistance (ohms/cm²):</td>
<td>23.9 (4.8)</td>
<td>30.3 (2.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Amiloride (10 µM):</td>
<td>-57.1% (5.4)</td>
<td>-56.4% (6.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Resistance (ohms/cm²):</td>
<td>-0.5% (1.9)</td>
<td>0.9% (5.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Isoprenaline (10 µM):</td>
<td>59.8% (14.9)</td>
<td>94.7% (8.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Resistance (ohms/cm²):</td>
<td>-0.5% (5.9)</td>
<td>3.5% (5.2)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Footnote as for table 2.

Table 4 Bioelectric properties of biopsies of bronchial mucosa from HLT lungs (CF and non-CF patients) and non-CF non-HLT controls: effects of mucosal amiloride and serosal isoprenaline

<table>
<thead>
<tr>
<th></th>
<th>HLT lungs (CF + non-CF)</th>
<th>Non-CF non-HLT controls</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isceq (µA/cm²)</td>
<td>9.4 (1.3)</td>
<td>18.6 (4.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Potential difference (mV):</td>
<td>0.24 (0.04)</td>
<td>0.34 (0.08)</td>
<td>NS</td>
</tr>
<tr>
<td>Resistance (ohms/cm²):</td>
<td>26.9 (2.8)</td>
<td>21.2 (3.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Amiloride (10 µM):</td>
<td>-56.8% (3.9)</td>
<td>-62.2% (14.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Resistance (ohms/cm²):</td>
<td>0.2% (2.8)</td>
<td>1.3% (2.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Isoprenaline (10 µM):</td>
<td>75.6% (10.2)</td>
<td>69.4% (10.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Resistance (ohms/cm²):</td>
<td>1.5% (3.8)</td>
<td>0.3% (4.8)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Footnote as for table 2.

Bacterial culture and cytomegaloviral immunofluorescence.

Transbronchial biopsies were performed for the surveillance of possible rejection and infection in the HLT recipients. Three biopsies were obtained with the flexible bronchoscopic biopsy forceps advanced to one of the basal segments of the lower lobe. Specimens were placed in formal saline, processed for histological examination and, if indicated, treated with Grocott silver stain for pneumocystis infection.

STATISTICAL METHODS

The Mann-Whitney U test was used to compare the basal values and pharmacological responses of the CF non-HLT subjects and non-CF non-HLT “controls”, CF and non-CF HLT recipients, the combined HLT subjects in comparison with non-CF non-HLT “controls”, and of the HLT patients with and without rejection. The null hypothesis was rejected at p < 0.05. Data are expressed as means (SE).

Results

NON-CF NON-HLT “CONTROLS” AND CF NON-HLT TISSUES

There were no significant differences in the basal bioelectric properties of bronchial mucosal tissue from non-CF non-HLT “controls” and CF non-HLT patients (table 2). The mean resistance of the 5 mm sheets in both non-CF and CF groups (63.8 and 54.1 ohms/cm²) was significantly higher, however, (p < 0.01) than both 3 mm sheets (27.7 and 26.7 ohms/cm²) and 3 mm biopsy tissues (21.2 and 20.9 ohms/cm², respectively).

In the non-CF non-HLT tissues, the application of mucosal amiloride (10 µM) caused a decrease in Isceq and subsequent stimulation with serosal isoprenaline (10 µM) produced a rise in Isceq (table 2). By contrast, the Isceq of CF non-HLT tissues showed a greater reduction after mucosal amiloride. The subsequent addition of serosal isoprenaline did not alter the Isceq (p < 0.05) compared with non-CF non-HLT tissues.

BIOPSYs FROM NON-CF HLT AND CF HLT PATIENTS

There were no significant differences in the basal bioelectric properties between the CF and non-CF biopsies of bronchial mucosa from the transplanted lungs (table 3). Addition of mucosal amiloride to non-CF HLT and CF HLT tissues caused a similar decrease in Isceq and subsequent stimulation with serosal isoprenaline led to an increase in Isceq that was not significantly different between the two groups (table 3).

BIOPSYs FROM HLT PATIENTS AND NON-CF NON-HLT “CONTROLS”

Because no differences were detected in the bioelectric properties and pharmacological responses of the mucosal biopsies between the CF and non-CF HLT patients, tissues were grouped together as “HLT lungs” (n = 11) and their properties compared with the 3 mm biopsies from the non-CF non-HLT “controls” (n = 5). No significant differences were found in the basal bioelectric properties of the two groups (table 4). Amiloride and isoprenaline produced similar changes in bioelectric properties of both groups (table 4).

Discussion

The altered bioelectric properties of CF tissues could be detected by the mini-Ussing chamber technique. The basal bioelectric values and the responses to amiloride and isoprenaline in patients with CF were not different from non-CF patients two years after HLT. No significant difference in the basal bioelectric properties and responses to
amiloride and isoprenaline was found between HLT recipients and non-CF non-HLT subjects.

After HLT, the airways of patients with CF show a similar profile in potential difference to non-CF patients, suggesting that the transplanted lungs have retained “normal” epithelial function.14 Such in vivo measurements are, however, necessarily limited. As the CF defect relates to abnormal regulation of ion transport, in vitro studies of biopsies of bronchial mucosa should be able to amplify these initial in vivo findings. In vitro characterisation of the bioelectric properties of bronchial tissue from humans is difficult, however, compared with studies of tissues from laboratory animals. We attempted to minimise several factors that might lead to artefactual bioelectric measurements. General anaesthesia, which did not seem to have any significant effect on airway potential difference, was used during the bronchoscopic procedures. This avoided any possible application of topical lignocaine on to the mucosal surface, shown to reduce the airway potential difference.20 Mucosal biopsies obtained for this study were placed in cold aerated Ringer solution without delay and transferred to the laboratory to minimise tissue hypoxia. In this study, the similarity of tissue responses to amiloride in vitro compared with in vivo data20 suggests that these tissues did not sustain significant hypoxic damage.21 Medications were similar in non-CF and CF HLT patients, except for vitamin and pancreatic enzyme supplements for the second group. The major difference between the HLT and non-HLT groups, however, was the treatment with cyclosporin to prevent rejection. This treatment has been shown to affect glucose and fatty acid uptake in normal rat bowel,14 and the effects of cyclosporin on transport across epithelial tissues require further examination.

Both the procedure for bronchoscopic biopsy itself and the process of clamping small tissues between the perspex plates of the mini-Ussing chamber may cause edge damage. This is supported by our finding that the 5 mm sheets had a significantly higher tissue resistance compared with the 3 mm sheets and biopsies. There have been similar findings in mini-Ussing chamber studies of human and rabbit rectal biopsies.18 These rectal preparations exhibit qualitatively the same pattern of responses to amiloride and acetylcholine, however, as that obtained with a larger sheet of rectal mucosa. In this study, the pharmacological responses of non-CF tissues were similar to those previously reported for tissues mounted in full size Ussing chambers.22 In CF tissues, the Isc responses to amiloride were greater than those of the non-CF sheets, as previously reported,22 although the difference did not reach statistical significance. Undoubtedly the use of mini-Ussing chambers and the necessary technical limitations imposed result in a greater variability than that seen with full sized chambers. Despite this, the characteristically reduced response to cyclic AMP stimulation in CF tissues was clearly seen.23

In patients with CF, the potential difference of the transplanted airways measured in vivo did not differ from that in non-CF transplanted patients up to two years after transplantation, although the nasal potential difference in the patients with CF remained abnormal.14 15 The potential difference profile of the lower airways in both CF and non-CF patients after transplantation was altered, however, compared with that of non-CF non-HLT patients. A more detailed characterisation of airway bioelectric properties was possible with the biopsy samples obtained from the HLT patients undergoing tranbronchial biopsy. No significant difference in the basal bioelectric properties was detected between biopsies obtained from CF and non-CF HLT patients. Furthermore, the profiles in response of biopsy tissues from the CF HLT patients to both amiloride and isoprenaline did not differ from those in tissues from non-CF HLT patients, up to two years after transplantation. Our results therefore confirm the previous in vivo findings on the potential difference in airways.

To assess the possibility that transplanted airways (CF and non-CF HLT patients), which were subjected to denervation, interruption of the bronchial arteries and lymphatic system, rejection, and infective episodes after HLT, might have different bioelectric properties, the non-CF non-HLT “control” patients were compared with HLT patients. Because the differences between bioelectric properties of mucosal biopsies from CF and non-CF HLT patients were not statistically significant, their values were averaged for comparison. For the bioelectric properties, no significant difference was detected between the HLT and non-HLT groups. Their pharmacological responses to amiloride and isoprenaline were similar and the profile of changes was similar to that of human bronchi obtained from lung resection.24 This suggests that the transplanted lungs retain functional epithelial integrity despite the surgical and immunological interventions. Also, lung denervation on its own does not seem to affect the airway potential difference in the cases of single lung transplantation.24 With the increasing use of bronchial artery revascularisation in isolated lung transplantation22 to improve bronchial anastomotic healing, this would provide an opportunity to study the effects of ischaemia on the bioelectric properties of the airways. In conclusion, we have shown the feasibility of studying the bioelectric properties of biopsy specimens of bronchial mucosa obtained at bronchoscopy. Up to two years after HLT, the properties of non-CF and CF tissues are indistinguishable and, in turn, neither group shows altered responses in comparison with non-HLT tissues.

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