The analysis of CFTR localisation, expression and function have been conducted on human and murine tissues and on native cells from healthy individuals and CF patients or on primary human and murine cell cultures as well as on diverse epithelial cell lines. Reliable experimental protocols are required for determining the relationship between normal CFTR expression and function as well as for analyzing the degree of CFTR mis-localisation in CF tissues and precisely controlling the capacity of therapeutics to modulate CFTR trafficking and induce its correct re-localisation.

The expression and localisation of wild-type- and F508del-CFTR have been frequently studied on nonpolarized heterologous expression systems and cell lines that may, to a certain extent, mimic correctly the normal or CF tissue. Even in native normal epithelial tissues, the endogenous expression of CFTR is tissue-specific and may differ according to the degree of differentiation of the epithelium. In CF affected tissues, the degree of epithelial inflammation and remodelling and the tissue-specific processing of the mutant CFTR protein may result in an apparent wild-type situation or in contrast, in a marked decrease of CFTR expression with a mis-localisation of CFTR protein. Therefore, the epithelial integrity (controlled by polarity and intercellular adhesion molecules markers) of the native epithelial tissue samples and the maintenance of well differentiated and polarized cell cultures are required for assessing correctly the CFTR expression and localisation.

In this section are regrouped techniques and experimental protocols for assessing CFTR localisation in human and murine tissues [1] and in native airway epithelial cells obtained by nasal brushings [2]. The optimal culture conditions for analyzing CFTR in human and murine airway cell cultures [3–5] including 2-D (air–liquid interface) and 3-D cultures [6] are also reported. A chimeric humanized xenograft tissue model that reconstitutes a fully differentiated human airway epithelium is described [7]. This in vivo model offers the unique opportunity to analyze CFTR localisation and expression during the different steps of airway epithelium differentiation and regeneration.

References