Section D (cell physiology): an armamentarium to investigate CFTR function

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The cystic fibrosis transmembrane conductance regulator (CFTR) [1] is a unique member of the ATP-binding cassette (ABC) transporter family that plays a central role in salt and liquid movements across epithelial tissues [2]. CFTR is a multifunctional protein: its best characterised function is as a Cl\(^{-}\) channel with complex regulation [3,4]. In addition, CFTR has been demonstrated to regulate the activity of other ion channels and transporters in epithelial cells [5]. Loss of these different functions of CFTR disrupts trans-epithelial electrolyte transport in a variety of organs to cause the wide-ranging manifestations characteristic of cystic fibrosis (CF) [2].

The Cell Physiology Section of the Online Virtual Repository of Methods and Reagents for CFTR Expression and Functional Studies (Section D) [6] contains consensus protocols on many of the different approaches that researchers employ to understand better CFTR and its dysfunction in disease. It also provides a catalogue of pharmacological reagents that can be used to modulate CFTR Cl\(^{-}\) currents. These protocols are not intended to be step-by-step instructions for researchers to follow when using specific techniques to study CFTR. Instead, their purpose is to provide valuable help and advice to novice and expert alike as they seek new knowledge and understanding of CFTR.

To investigate the different functions of CFTR, a rich variety of materials and methods are used. The activity of wild-type and mutant CFTR is studied in native tissues and heterologous expression systems at the molecular, cellular and tissue levels. Many of the methods are electrophysiological ranging from high-resolution recording of individual CFTR Cl\(^{-}\) channels using the patch-clamp technique [7] to Cl\(^{-}\) flow across polarised epithelia monitored with the Ussing chamber technique [8]. Other methods employ planar lipid bilayers and ATPases assays to understand, at the molecular level, how ATP hydrolysis drives conformation changes in the CFTR Cl\(^{-}\) channel [7,9]. Yet other methods employ fluorescent dyes and radioisotopes to assay the function of CFTR in populations of cells [10,11]. Finally, innovative techniques using confocal and electron microscopy have been developed to investigate the pathogenesis of CF lung disease [12].

The following articles provide an overview of the rich variety of protocols in the Cell Physiology Section of the Online Virtual Repository of Methods and Reagents for CFTR Expression and Functional Studies [6] compiled by the European Working Group on CFTR Expression. We encourage you strongly to visit the Online Virtual Repository and examine in detail the protocols.

References


