Current Topics in Membranes and Transport

VOLUME 20

MOLECULAR APPROACHES TO EPITHELIAL TRANSPORT

Guest Editors

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Preface

In recent years the issues in epithelial transport research have gradually evolved toward the molecular level. As recently as ten years ago, the predominant problem was to determine exactly what electrolytes and nonelectrolytes particular epithelia absorb or secrete. Once armed with an understanding of the macroscopic transport processes, researchers asked whether the movement of substances was through the cells (i.e., active) or between the cells (i.e., passive) flowing along favorable electrical and/or chemical gradients. In turn, using electrical or chemical methods, the question was raised at which step in transcellular transport was energy in the form of ATP required. As an example, in transepithelial sodium transport, sodium enters the cell passively down a net electrochemical gradient and is actively extruded into the blood via an ATP-requiring transport protein (the Na^+,K^+-ATPase). One of the most recent topics being addressed is the mechanism involved in the regulation of these electrolyte and nonelectrolyte transport proteins (synthesis and/or activation), and whether such proteins move substances by a channel-type configuration or a carrier configuration.

It is obvious that the more classic approaches to studying epithelial transport are inadequate by themselves to address these questions fully. It is the purpose of this book to outline and illustrate, by example, some recently developed approaches that can provide important new insight into epithelial transport mechanisms.

Part I of this volume is devoted to the electrical methodology used to address questions such as the following: Does sodium entry across the apical membrane of tight epithelia occur by a channel or carrier mechanism? Do hormones increase the number of transport proteins or the ability of a single protein to carry more ions per unit time? During stimulation of ion transport, are quiescent channels activated, or are cytoplasmic vesicles containing the transport protein mobilized on a certain signal and inserted into the membrane? The methods to be used consist of impedance analysis to measure changes in membrane area associated with stimulation of transport and fluctuation analysis to evaluate alterations in channel density.

Part II provides a wide range of examples of how antibodies to epithelial membrane proteins can be useful. Antibodies are clearly a powerful tool for evaluating the biosynthesis of transport proteins such as Na^+,K^+-ATPase and

provide a means whereby membrane proteins can be identified and localized in epithelia.

Part III of the volume describes biochemical approaches to characterizing epithelial transport systems. These chapters illustrate approaches being taken for isolation and identification of transport proteins. In addition, these studies show how substrate protection can be utilized to identify chemical groups associated with important sites of a transport system.

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JAMES B. WADE
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Contents

Part I

Frequency Domain Analysis of Ion Transport

Chapter 1

Fluctuation Analysis of Apical Sodium Transport

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I. INTRODUCTION

Fluctuation analysis has been used in the study of nerve and black lipid membranes for several years now, but it is only fairly recently that much has been accomplished in epithelial membranes using this technique. The complexity of epithelial membranes has been perhaps the primary deterrent. Four years ago I described some of the very early results (Hoshiko and Moore, 1978) as did Lindemann and Van Driessche (1978). Lindemann has subsequently reviewed work to 1980 (Lindemann, 1980). Since then two types of models for interpreta-

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