
Preface

Membrane proteins are essential components of biological processes such as ions, metabolites or water transport, signal transduction, sensing cell environment, and control of cell-cell contact. Dysfunction of these proteins induces numerous human pathologies like cystic fibrosis which originates from a genetic disorder that is linked to the most common case to the deletion of one amino acid. Many other disorders like cancers and inflammatory diseases occur through cell-cell communications and involve membrane proteins.

Although many studies have been performed to characterize membrane proteins, there is a lack of information upon this class of proteins both in terms of structures and function. One of the bottlenecks is the low abundance of these proteins in native membranes, making difficult the characterization and the study of their function. To overcome this difficulty, overexpression in various systems has gained increasing interest over the last decades, leading, in particular, to the production of sufficient amounts for structural studies. Although the number of high resolution structures of membrane proteins has increased, it remains well below that of soluble proteins.

Some membrane proteins have been easily overexpressed, but it is not a common case. Expression remains challenging especially for mammalian proteins compared to bacterial ones, the former often requiring molecular chaperones to fold correctly, and post-translational modifications to be functional. This volume addresses different approaches to produce membrane proteins, to purify them, to verify their function, to determine their structure, and to model them in membrane. Since every membrane protein behaves mostly in a unique way, knowledge of guidelines and tricks may help to increase chances to express, purify, and characterize a peculiar membrane protein. Production of correctly folded protein remains a challenge. Moreover, getting a functional and stable protein requires optimizing membrane mimicking environments that can be detergent or artificial membranes. In some cases, the finding of the correct ligand that will stabilize the desired conformation is needed. In other cases, stabilization can be obtained using specific antibodies. This volume also presents different techniques to analyze the functional status of membrane proteins.

Recent progresses in structural biology of membrane proteins are described using examples for the main approaches that are electron microscopy, X-Ray diffraction, nuclear magnetic resonance (NMR), and bioinformatic computing. The new detector used for electron microscopes has increased resolution gained from either two-dimensional crystals or single particles. X-Ray free electron laser has permit to get high resolution structures using micron-size crystals. Solid-state NMR study gives de novo atomic structure of low molecular weight membrane proteins reconstituted in liposomes, but only spectral fingerprints of larger proteins. Recent developments in computing both from computer power (hardware) and from algorithms (software) have made possible molecular dynamics of larger membrane proteins at timescales compatible with conformational changes in the millisecond range. Structure-based drug design is a reality for membrane proteins in a close-to-native environment.

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Characterization

Methods and Protocols

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