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Membrane Proteins – Introduction

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Biomembranes are crucial components in the genesis of life and the structuring elements of the organisation of living cells. They preserve the functional integrity of cell organelles and regulate the exchange of solutes and signals between the different functional areas of the cell. Membrane proteins, which constitute about 30% of the entire protein content of the cell, are often very complex and function in many different ways. A large number of today's drugs are targeted at membrane proteins. In spite of their importance in modern life sciences, the structure and function of membrane proteins are not well understood, and only few membrane proteins have been investigated in detail. For example, among all protein structures deposited in the protein data bank, membrane protein structures represent only a very small fraction. The reasons for our restricted knowledge of membrane protein assembly, structure and function are limited technologies to express membrane proteins in large quantities, only very little insight into the assembly and folding of membrane proteins and insufficient knowledge how to handle membrane proteins in vitro to study their structure and function in a clearly defined environment without inactivating them. These difficulties arise from the hydrophobic nature of membrane proteins, which have to be transferred into aqueous solution to be accessible for spectroscopic and crystallographic studies on their structure and function.

The first three articles of this review series therefore address questions of membrane protein expression, assembly and stability. While membrane proteins from bacteria can be successfully overexpressed in *Escherichia coli*, overexpression of eukaryotic membrane proteins is more difficult. Eukaryotic membrane proteins, for example G-protein coupled receptors, which are important for transmembrane signal transduction, often serve as drug targets. The first review article by Alain Milon and co-authors presents currently employed expression systems for this important family among the α-helix-bundle transmembrane proteins.

The second review reports on the assembly of membrane proteins of the β-barrel type, which represent one of the two known structural classes, based on the example of outer membrane protein A. β-Barrel membrane proteins of known high-resolution structure are found in the outer membranes of prokaryotes, and similar β-barrel structures are predicted for membrane proteins of the outer membranes of mitochondria and chloroplasts.

For structure and function studies, membrane proteins are classically solubilized in detergent micelles. The properties of detergent micelles, however, are not ideal to keep membrane proteins in a thermodynamically stable, functionally active state. Therefore, novel approaches to keep membrane proteins stable in solution have been developed using non-detergent surfactants, for example amphipathic polymers, as alternatives to detergents. Amphipathic polymers provide several advantages over detergents in keeping membrane proteins soluble and preserving their activity for structural and functional characterization. Jean-Luc Popot and co-authors describe the progress made in this research area.

Biomembranes are composed of a large variety of lipids, which in addition to structuring the cell into the different functional units provide a liquid-crystalline host matrix for integral membrane proteins. The lipid compositions of various biomembranes are different for prokaryotic, plant and animal cells. The interactions of membrane lipids with integral membrane proteins and modulation of lipid chain ordering at the protein-lipid interface are important for membrane protein function. The review article by Derek Marsh gives an overview of lipid chain orientations observed in crystals by X-ray crystallography and in solution by ^{2}H-nuclear magnetic resonance spectroscopy and X-ray diffraction.

The potassium channel KcsA, which consists of two transmembrane α-helices and forms tetramers, is one of the few α-helical transmembrane proteins of known high-resolution crystal structure. There is strong evidence that the pore structure of this channel is similar to that of other potassium channels. The KcsA channel has been extensively studied by crystallographic and spectroscopic stud-

ies, and recent research articles have given much insight into ion channel function. Anthony Lee and co-authors review the structure, function and lipid protein interactions of this interesting ion channel.

The special lipid compositions of plant membranes indicate that lipid protein interactions are important for the function of membrane proteins. Recent work revealed that interactions of the nonbilayer lipid monogalactosyldiacylglycerol with the main light-harvesting chlorophyll a/b-binding protein complexes of photosystem-II play multiple structural and functional roles in the development and maturation of thylakoid membranes. Tibor Páli and co-authors review the functional significance of the lipid protein interface in photosynthetic membranes such as the thylakoid membrane in the final review article of this series.