Multi-author Review

Pore-forming proteins of biological membranes

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Introduction

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Biological membranes which separate different intra- and extracellular compartments from each other are necessarily barriers for a large number of substances. Apart from hydrophobic molecules only water and gases like CO_2, O_2 and N_2 permeate phospholipid bilayers by simple diffusion. Since most biological membranes (e.g. the plasma membrane, the inner membrane of mitochondria and bacteria, the ER membrane) have evolved to maintain ion gradients between different compartments, highly specific transport mechanisms are necessary which will allow single molecules selectively to cross the membrane. Specificity is achieved with the aid of a transport protein which 'recognizes' only one substance and either helps its diffusion through the membrane (= *passive transport*, facilitated diffusion), or actively 'pumps' the molecule into another compartment with the consumption of ATP, or transports one molecule at the expense of another (= *active transport* through ATPases or symport/antiport) in which case a gradient can be established.

The outer membranes of bacteria and of mitochondria are exceptional in that they need to maintain neither a gradient nor an electrochemical potential. In fact, their permeability to a variety of hydrophilic substances makes them appear like molecular sieves. The actual 'holes' in the outer membrane are formed by channel proteins called 'porins' in both prokaryotes and mitochondria. They are analogous in their function, but do not share any sequence homology. Since these pores are large and water-filled, hydrophilic substances are thought to permeate through them by simple diffusion. Equally non-specific but completely different in their structure and mechanism of action are killer-pores which are known as 'colicins' in prokaryotes and 'killer-toxin' of virus-like particles in eukaryotes (yeasts). In both cases a secreted protein becomes toxic by being inserted into a foreign membrane and destroying its potential via channel-formation.

How do all these pores work in detail? How are they synthesized and what is their importance in vivo? What are the features common to both prokaryotic and eukaryotic pores? The following reviews attempt to give up-to-date answers to these questions in discussing the structure, function and biogenesis of different eukaryotic and prokaryotic non-specific pore proteins.

Biophysical properties of porin pores from mitochondrial outer membrane of eukaryotic cells

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Summary. The matrix space of mitochondria is surrounded by two membranes. The mitochondrial inner membrane contains the respiration chain and a large number of highly specific carriers for the mostly anionic substrates of mitochondrial metabolism. In contrast to this the permeability properties of the mitochondrial outer membrane are by far less specific. It acts as a molecular sieve for hydrophilic molecules with a defined exclusion limit around 3000 Da. Responsible for the extremely high permeability of the mitochondrial outer membrane is the presence of a pore-forming protein termed mitochondrial porin. Mitochondrial porins have been isolated from a variety of eukaryotic cells. They are basic proteins with molecular masses between 30 and 35 kDa. Reconstitution experiments define their function as pore-forming components with a single-channel conductance of about 0.40 nS (nano Siemens) in 0.1 M KCl at low voltages. In the open state mitochondrial porin behaves as a general diffusion pore with an effective diameter of 1.7 nm. Eukaryotic porins are slightly anion-selective in the open state but become cation-selective after voltage-dependent closure.

Key words. Mitochondria; outer membrane; voltage-dependence; single-channel conductance; lipid bilayer membrane; reconstitution.