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Structure and function of colicin A and N

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The lipid bilayer membrane which surrounds living cells is a very effective barrier in preventing diffusion of small molecules and macromolecules into the cytoplasm. In order to reach their site of action inside the target cells, from their site of synthesis within the producing cell, toxins must cross two to four membranes. How these macromolecules are able to cross these barriers is a central question which is still far from being understood. One large class of toxins exerts its lethal effect by inserting into the target cell membranes and forming a pore which perturbs the ionic and osmotic balance across the membrane, inducing a wide diversity of biological effects such as loss of solute, inhibition of active transport, depolarization of the membrane, and arrest of protein synthesis. These toxins are produced in a water soluble form which is able to diffuse towards the target cell in an aqueous environment. But in their final state, the pore, they become integral membrane proteins embeded in the hydrophobic core of a lipid bilayer. How a single polypeptide chain can first cross a membrane and then insert into a second membrane to form a voltage gated channel is the question we have been addressing for many years by studying the pore-forming colicins A and N.

Colicins are plasmid encoded bacteriocins produced by *E. coli* which kill sensitive *E. coli* strains and related bacteria. The cell enveloppe of gram negative bacteria with its two membranes presents a serious obstacle for the uptake of macromolecules of the size of colicins (40-60 kDa). To cross this barrier and reach their target colicins first bind to their cognate receptor on the cell surface and then translocate through the outer membrane. The pore forming colicins (E1, A, B, N, Ia, IB, K, 10, 5) then insert into the inner membrane Uptake of colicins through the outer membrane follows two alternative pathways mediated by the Ton or the Tol system. The Ton system consists of the proteins TonB, ExbB and ExbD and is also invoved in the energy-dependent uptake of vitamin B12 and iron siderophores.and the Tol system consists of 6 proteins: TolA, TolB TolQ and TolR, PAL and Orf2. Colicins B, D, Ia, IB, M, 5 and 10 (group B) are taken up via the Ton pathway, whereas the translocation of group A colicins (colicin A, the E colicins, colicin K, N and cloacin DF13) involves interaction with TolA and different combinations of the proteins from the Tol family

The structures and mode of action of colicin A and N is the topic of this presentation with special emphasis on the réceptor/colicin interaction on the outer membrane of the bacteria.