Insertion of the Outer Membrane Protein F (OmpF) into asymmetric bilayers and antibiotic permeation

Annemarie Brauser[1,2], Thomas Gutsmann[2] and Mathias Winterhalter[1]

[1]Jacobs University Bremen, School of Engineering and Science, Biophysical Chemistry, Bremen, Germany; [2]Research Center Borstel, Leibniz-Center for Medicine and Biosciences, Immunochemistry and Biochemical Microbiology, Division of Biophysics, Borstel, Germany

More and more bacteria are resistant against classical antibiotics. For a better understanding how bacteria interact with classical antibiotics we focus on the mechanism of antibiotic transport through the outer membrane protein F (OmpF) and the intercalation of this protein into Montal-Mueller-membranes containing different types of LPS. Additionally, we determine the effect of the antimicrobial peptide LL20 on the intercalation of the porin into the membranes. The model membranes are asymmetric and contain Lipopolysaccharides (LPS) on one side and a phospholipid (PL) mixture on the other side. The used method was the Montal-Mueller technique.

The first results showed that the OmpF intercalates into the asymmetric membranes only from the PL side and the intercalation is much better in the presence of the antimicrobial peptide LL20 added to the LPS side. LL20 is a 20 amino acid fragment of the antimicrobial peptide cathelicidin LL-37.

The orientation of the OmpF in the experiments is not influenced by the LPS. The orientation is the same in both, symmetric and asymmetric membranes.

The single molecule measurements of OmpF and the transport of antibiotics through the channel showed different results from total blockage of the porin up to concentration dependent single blocking events. The LPS type which were used for the first experiments were from the *E. coli* strain WBB01, *S. ent.* Minn. strain R595 and *P. mirabilis* strain R45 which are deep rough mutants containing only two 2-keto-3-deoxyoctulosonic acid (Kdo) and no core region or O-specific chain. The LPS from the strain R45 has additional aminoarabinose bound to one of the first Kdo and to one of the phosphate groups.