Protein-membrane interactions and protein-protein recognition within the membrane milieu are of fundamental importance to fully comprehend a wide range of cellular processes in all organisms. About 40% of all genes in the mammalian genome transcribe for membrane proteins. The paucity in 3D structures for most membrane proteins, the high complexity of the forces involved, and the technical difficulties present challenging obstacles to overcome before fully understanding biological events within membranes. Using a multidisciplinary approach, including cell biology (cells and viruses), biophysics and chemistry, we studied the mode of action of membrane proteins, particularly those involved in infectious diseases. These studies led us to discover and refine mechanisms of action of membrane proteins involved in microbial and viral infections.

Antimicrobial peptides in Innate Immunity: The Underlying Parameters Involved in Target Recognition by Antimicrobial Peptides

Living organisms of all types including plants and humans have been shown to produce a large repertoire of gene-encoded antimicrobial peptides that serve as part of their innate immunity to microbial invasion. They are considered as future antibiotics due to the increasing resistance of bacteria to available antibiotics. We established the carpet (Fig. 1) mechanism as an efficient model describing action of antimicrobial peptides. Based on this mechanism we developed a novel repertoire of diastereomeric antimicrobial peptides with potential therapeutic applications.

Viral Infection - How do Viral Envelope Proteins Catalyze Viral-Cell Membrane Fusion?

The mechanism by which specific viral envelope proteins catalyze mixing of two membranes (membrane fusion) is still an open question. We focused on gp41 and F, the envelope glycoproteins from HIV (retrovirus) and Sendai virus (paramyxovirus), respectively. We show that: (i) distant viral families share conserved fusion mechanisms, (ii) membrane interaction induces drastic conformational changes in the fusion proteins. These studies led us to propose the umbrella (Fig. 2) mechanism for virus-cell fusion. (iii) Synthetic peptides derived from envelope proteins specifically inhibit viral infection at different stages, making them ideal tools for mechanism studies, as well as promising therapeutic agents.

General Aspects on Protein-Membrane and Protein-Protein Interactions within the Membrane

We studied self- and hetero-assembly of peptides within the membrane milieu. In contrast to recognition in solution, we found that peptide chirality does not affect protein-protein recognition in the membrane, and therefore biological function is preserved. Furthermore, we developed a new assay that allows for the first time in vivo detection of hetero-association between proteins within the membrane milieu. Besides giving us important basic information, these findings serve as new tools for the design of novel compounds to combat infectious diseases.
Selected Publications


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