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PREFACE

# Viral membrane proteins

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This special issue on 'Viral membrane proteins' incorporates a series of research articles that were presented at the 'Conference on Viral Membrane Proteins', held at the University of Heidelberg, Germany, on 12–14 December 2008. The aim of the symposium was to involve all areas of research in this emerging field focusing on biophysical and clinically relevant approaches as well as on the fundamental science.

The interest in viral membrane proteins has different foundations. The most obvious is that viral membrane proteins can serve as targets for a new generation of antiviral drugs. But in addition to this, viral membrane proteins reveal many unique structural and functional features that can provide a blueprint for developing molecular tools for bio- and nanotechnology as well as biomedicine.

Whilst the membrane proteins of the host comprise up to 50% of all drug targets, this frequency is not yet the case for viral membrane proteins. Today most antiviral drugs target globular proteins with only a few targeting membrane proteins. To highlight some of these membrane proteins: they include entry inhibitors for HIV-1 and influenza as well as channel blockers for the latter virus. A better understanding of the role and also of the structure of viral membrane proteins can be anticipated to be directly relevant for the assessment of these proteins as potential drug targets in the very near future. At the current state of knowledge, viral membrane proteins in particular are very likely to become very important drug targets, as an increasing number of companies are dealing with this type of protein.

Apart from their role as drug targets, viral membrane proteins also have many other interesting features. They may, for example, serve as templates for unique techniques for proteinaceous systems which enable the delivery of large cargo across the lipid membrane. The "technology" used by the viruses includes fusion and transduction. Some viruses have coupled membrane protein-based sensor systems including proteins that ultimately perform the fusion event. One such coupled protein system is the neuraminidase (sensor)/hemaglutinin (fusion) system of influenza. Other viruses such as HIV-1 have non-covalently linked their fusion machinery, gp41, with a sensor protein, gp120, with the latter placed like a backpack on top of the former. A completely different strategy relies on formation of channels and pores that facilitate the flux of the viral genome into the cell (polio virus, tobacco mosaic virus). In the case of transduction, certain sequences of viral proteins are highly enriched with positively charged amino acids known to facilitate transduction. Used as a short sequence, these positively charged peptides may work as artificial vehicles for cargo delivery across the lipid membrane.

Whatever one's interest in viral membrane proteins is, whether it is as a drug target or a shuttle system, the first, most essential step is to achieve a profound understanding of the structural and functional aspects of these proteins. To achieve the necessary level of understanding, a broad range of techniques has to be employed in the investigation of the proteins. Since all techniques cover specific time and size

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scales and contribute to piecing together the puzzle of the mechanism by which these proteins function, there is a pressing need to gather and share the experiences and the results amongst the individual research communities. The goal for the future is to further link all the evidence together with the wish to answer some of the ever important questions such as (1) how these proteins work on an atomic level, (2) what makes them multi-tasking, and (3) how their mode of action can be hampered.

The conference was held within the framework of a DFG/NSC Bilateral Symposium supported by the German Research Council (DFG) and the National Science Council of Taiwan (NSC). It should be noted that the conference was preceded by earlier international conferences, e.g. in Italy and Taiwan, on the same topic. We wish to take the pressure we are facing from these viruses that present a continuous threat and those that lurk at the species barrier as an incitement and impetus for further meetings.