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Preface

Introduction to the Special Issue 'Viral Membrane Proteins — Channels for Cellular Networking'

This special issue emerges from a symposium held on Viral Membrane Proteins in Taipei, TW, in 2012. The goal of the conference was to identify and characterize novel and existing viral channel forming proteins (VCPs), as well as to address the question of how these proteins interact with host factors. Prof. Harald zur Hausen, Nobel Laureate in Medicine in 2008, joined the symposium as a keynote speaker, introducing the pathology of papilloma viruses, which is the 'latest' virus harboring the code for a VCP: "I am happy having joined the symposium and seeing the integrative approach amongst disciplines on a successful road towards a better understanding of viral activity and its consequences for the cure of infection."

In a previous issue in 2011, we have reported about VCPs, which are identified to self-assemble into homo-oligomers and support the viral infectivity cycle by enabling ion or substrate flux across the lipid membrane (BBA-2011). Due to the fact that some of them are found to conduct small molecular weight compounds, these proteins are also categorized as 'viroporins'.

When viruses invade the host cell they have to fulfill an enormous amount of tasks in order to make the host a comfortable place for self-replication. They have to cross lipid membranes and alter membrane dynamics and shape, change electrochemical environments within the cell or block the mode of action of host proteins. It seems that the numerous tasks need an endless number of tools. However, retroviral genomes (of human viruses) are small and consequently it is assumed, that some proteins may have multiple roles rather than a single one.

The consequences of the mode of actions, e.g. changing electrochemical gradients, are in some cases clearly identified to VCPs. In this respect, M2 from influenza A, allows protons to cross the membrane when sensing a gradient. Thus, its duty is to 'wake-up' hemagglutinin, a viral membrane protein companion within the envelope of the virion, once the virus is trapped within the endosome *via* protonation. Within the infected cell, M2 also takes care that hemagglutinin is getting into its functional form during the manufacturing process in the endoplasmic reticulum.

On the other end of the scale is e.g. Vpu of HIV-1. Vpu is known to form channels when reconstituted into artificial lipid membranes or expressed in *Xenopus* oocytes, but its role is hence to be identified unanimously. It is proposed, that it amplifies viral release at the site of the plasma membrane, when the newly formed virions aim to escape the cell. The general idea is, that localized gradients develop when the two membranes approach each other during pinching-off, and the viral channel releases the gradient, locally lowering the ion strength between the approaching membrane parts. This mechanism of ction is seen to be the role for the viral potassium channels in plant viruses (Kcv of PBCV-1). Yet, for Vpu, this idea shattered when reports came up showing that Vpu rather interacts with BST-2, a human 'pinching-off blocker' activated during viral infection. Discoveries about Vpu-BST-2 interactions were soon followed by reports that BST-2 is not the only 'partner' with which Vpu interacts. Now, what is going on here? Is Vpu another 'Pluto'? Has the protein to be expelled from the 'club'?

Some backing of Vpu is coming from the proposal of a novel channel protein E5 of HPV. This protein is known to interact with a number of host factors in order to tune the cell into a comfortable place for HPV in the first place. It is just since 2011, that it has entered the 'club'. With this in mind we can carry on asking, whether there are more of the known channels to be host protein modulators. In many cases the membership in the club is claimed prior to a full identification of the role of the protein within the life cycle of the virus.

With these examples, a series of new questions about the mechanism of function of these channels as 'multi-tasking' tools arise. Do they act in distinct conformations and oligomeric states when assembling with themselves or with host factors? More generally, what is the molecular basis for the decision making process about with whom to assemble?

The special issue contains reviews on the VCPs and also on interactions with host factors known to date. VCPs are characterized and results about finding drugs against one of the channels are presented. This issue also includes novel findings on fusion proteins and other viral membrane proteins. Contributions from computational and biophotonics research is included to outline the techniques with which the viruses and their proteins can be addressed.

Let us express our warmest thanks to all the researchers bringing this issue alive. At this stage we thank the editorial team of BBA for their continuous excellent support.

Wolfgang B. Fischer, PhD in Chemistry, Heidelberg University, entered the field of membrane proteins during his time as a Postdoc at Boston University, MA, USA, and later at TU Dresden, D. He worked on bacteriophodopsin and the nicotinic acetylcholine receptor, respectively, using FTIR spectroscopy. During his stay as a Marie Curie EU-Fellow and later as lecturer at Oxford University, UK, he moved into structure based computer simulations of membrane proteins focusing on viral channel forming proteins. His main achievements are structural proposals for a series of viral proteins such as Vpu of HIV-1, p7 of HCV and 2B of poliovirus. At National Yang-Ming University he discovered 8a from SARS-CoV to be a viral channel protein, using conductance measurements and proposed a first computer based structural model of the assembled protein. His research focuses on the mode of oligomerisation of these membrane proteins within the lipid bilayer and the initiation of ion and substrate flux through these channels. In addition, assembly with host factors is investigated.

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