The viruses' view of the cell – cell biology using viruses as probes

Meeting Report on the 8th Workshop ‚Cell Biology of Viral Infections' of the German Society of Virology (GfV) in Deidesheim, October 5th-7th 2009.

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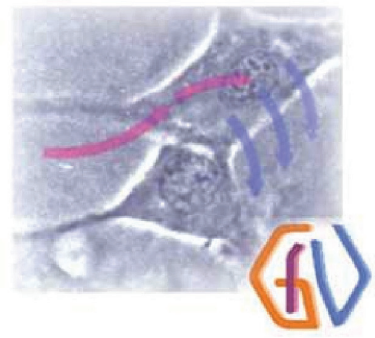

Viruses are not living organisms in a strict sense, but are obligatorily dependent on cells to replicate and to fulfil their 'life cycles'. Towards this end, viruses exploit a large variety of basic cellular processes such as endocytosis, nuclear import, transcription, replication, and exocytosis. Early cell biological studies made use of viruses as they provided a simple, limited component system that could be easily followed by the molecular biological, biochemical, and morphological techniques available. With the technological advances made over the decades, cell biologists expanded their model systems and toolkits, and pathogens ceased to be a major tool to study cellular biology. However, this field at the crossroad between cell biology and infection biology has re-emerged with new vigour particularly in membrane traffic [1-4], for overviews refer to [5-8].

To foster exchange and research at the crossroads of cell biology and virology, the German Society of Virology established the study group ‚Cell Biology of Viral Infections'. The main purpose of this study group is to bring together researchers of the allegedly divided fields by means of informal workshops. Held again on the estates of the famous winery Basserman-Jordan (Deidesheim) in the palatinate region, last year's 8th annual workshop was again generously co-sponsored by the German Society of Cell Biology. Four cell biological keynote speakers gave exciting insights into their particular research efforts.

Mark Marsh from the MRC-Laboratory of Molecular Cell Biology at the University College London re-visited lentivirus assembly focusing on fidelity and pathogenesis. He described the involvement of the cellular ESCRT machinery, the specific role of its different components in the viral assembly process, and he made the comparison to their genuine cellular function. He pointed out the similarity in membrane topologies for the structures budding away from the cytosol in the formation of multivesicular bodies and retrovirus budding. His presentation, moreover, summarized the importance of following membrane continuities over long distances to reveal the nature of a compartment that on a first look might appear endosomal but was revealed to be a complex invagination of the plasma membrane.

Volker Haucke (FU Berlin) talked about the regulation of adaptor-mediated membrane dynamics with a focus on clathrin-mediated endocytosis. This regulation is highly complex and involves the crosstalk of various cellular signalling pathways. Additionally, he emphasized the differences between clathrin coats on the plasma membrane and those on other intracellular compartments. Throughout his talk, he summarized the contribution of a wide range of methodological approaches that have contributed to our current understanding of the processes involved.

Jonathon Howard from the MPI of Molecular Cell Biology and Genetics (Dresden) gave an entertaining and insightful talk on the motor protein family of kinesins and their interaction with the cytoskeleton. He clearly laid out the many uses of these engines. This covered the mechanisms by which the proteins convert chemical energy derived from the hydrolysis of ATP into mechanical work, how this is used to move along microtubules but also to depolymerize microtubules. The dynamic properties of this system required the combination of several dedicated techniques - single-molecule fluorescence, optical tweezers, image processing, modelling, molecular biology, nanofabrication and nanofluidics, and electron microscopy. Integrating the results helped to understand the self-organization of molecules into organelles and interactions that constitute a form of mechanical signalling.

Finally, *Marius Lemberg* from the ZMBH, Heidelberg highlighted the mechanism and function of intramembrane proteases. While cytosolic or secreted proteases are rather well understood and most biologists are aware of their basic functions, intramembrane proteases as the name suggests act within membranes and such have more specific functions. Given that many signalling pathways receive their signals from a membrane surface and such the majority of the elements of a signalling cascade are integral or proximal to this membrane, these proteases have an import role in the regulation of cellular functions by cutting proteins within the lipid bilayer. At the same time, these proteases have to be regulated themselves. The presentation, again covering results stemming from a wide range of approaches, provided valuable insights into these complex

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networks and crosstalks. The following discussion visualized the challenges that a virus faces when successfully hijacking and modulating this complexity.

Besides the invited speakers, the participants displayed in a number of talks the wide variety of cell biological features of viral infections. The four sessions 'Organelles, membranes and membrane traffic', Cytoskeleton', 'All around the nucleus', and 'Cells and tissues' covered topics ranging from molecular details of single open membrane sheet generation during vaccinia virus assembly, analysis of virus induced and modulated signalling (Influenza A, Adenovirus, HIV) to modulation of host cell tissue changing e.g. polarity and barrier functions (Adeno- and Herpesviruses) - just to name a few. That for the first time a dedicated session on tissues was included, certainly provided the meeting with a wider scope. The talks also represented a wide expertise in techniques covering a range from specialized life cell imaging at cutting edge speed and sensitivity, small molecule techniques, RNAi screens, proteomics and electron microscopy, with the latter spanning from advanced immunolabelling, tomography to high resolution cryo electron microscopy.

The meeting proved again to be a platform that stimulated interdisciplinary discussions, provided valuable feedback and served as a nucleation point for a number of new collaborations. Among the presentations there were a number of studies that had emerged during discussions at earlier meetings. This year, we explored the source of the excellent Riesling in a guided vineyard walk followed by a wine tasting – this social event served once again as a stimulant for the scientific discussions. We hope this year´s 9th workshop will be similarly successful – and in order to make it happen, we would like to emphasize and explicitly extend our invitation to all researchers in fields of cell biology as well as pathogen-modulated host cell behaviour to join us from 29th September to 1st October 2010, again in Deidesheim. We take the committed participation in the discussions by the cell biological keynote speakers as clear sign that the covered aspects are by far not just of interest to virologists. Notably, among the best-received and –discussed talks was one by Miriam Stoeber from the Helenius lab at the ETH Zurich covering a pure cell biological topic. We are sure that this series of workshops will continue to stimulate interactions between researchers, both, with cell biological and virological interest.

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