10th anniversary of the GfV workshop "Cell Biology of viral infections" 2011

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Participants of the Workshop 2011

Since several years, the study section "Cell Biology of viral infections" of the German Society of Virology (GfV) has been organizing an annual meeting held at the Ketschauer Hof in Deidesheim, Pfalz. This workshop aims to bring together cell biologists and virologists with the view to foster collaborations and cell biological analysis of virus infections. This year, we celebrated the 10th anniversary of the workshop, which was founded in 2001 by Beate Sodeik and Michael Kann at Zeilitzheim, Würzburg. To commemorate the anniversary, the traditional wine tasting was a particularly festive one, organized in the vineyards and the cellar of the winery "Reichsrat von Buhl", Deidesheim.

The meeting took place September 21st to 23rd 2011 and focused on the "Modification of gene expression" (Fig. 1). Four keynote speakers were invited and presented overviews of their current work; they were a valuable contribution to a meeting that was up-to-date, very informative, well attended and lively. Interestingly, several keynote speakers did not know each other beforehand, which led to an unexpected side-effect, they made useful scientific contacts too. Meeting in a pleasant and rather intimate setting, the "cell-biologists" had ample time to converse and exchange ideas, which sparked their interest in mutual co-operations.

Stefan Hüttelmaier is professor of Molecular Cell Biology and director of the Core Facility Imaging at the Martin-Luther-University Halle-Wittenberg. His lecture "A guided tour for mRNAs: Posttranscriptional control of cell migration" focused on the current knowledge and state-of-the-art analysis of the spatio-temporal distribution of mRNAs. Specific eukaryotic mRNAs seem to be inhibited translationally until they reach the subcellular region where their protein products are needed. A well known example is the transcript encoding β-actin (ACTB). β-actin is critically involved in modulation of plasmamembrane extensions like exploratory growth cones of neurons and lamellipodia of fibroblasts. To ensure the regulated expression of β-actin at sites highly active in cell migration, premature translation of the transported ACTB mRNA is prevented by the ACTB mRNA binding protein ZBP1 (Zipcode binding protein 1). Intracellular signalling activates regulatory kinases that phosphorylate ZBP1 which triggers its release from the ACTB mRNA and initiates regulated and local synthesis of β-actin. Additional mechanisms to control translation of mRNAs were described by Stefan Hüttelmaier that enhance dynamics of the actin cytoskeleton and allow the control of cell polarization.

The research of **Gunter Meister**, head of the department of biochemistry at the University of Regensburg, focuses on the analysis of small regulatory or non-coding RNAs involved in regulation of gene expression. In his plenary talk on the "Mechanisms of microRNA-guided gene silencing" he provided an overview on various small RNAs, their biogenesis and influence on gene expression. Along with short interfering RNAs (siRNAs), microRNAs (miRNAs) are the most important members of this class of RNAs. While siRNAs are synthetic, exogenously introduced RNAs, miRNAs are processed products of cellular transripts. Gene repression by miRNAs is moderately efficient suggesting a role in fine-tuning the transcriptional activity to dynamically adjust for protein needs. The advent of deep sequencing led to the discovery of numerous other regulatory small RNAs originating from longer non-coding RNAs like tRNAs or snoRNAs, transposable elements or heterochromatic regions, a research area that is only evolving now. Future studies will focus on the mechanism of small regulatory RNAs to specifically regulate gene expression which makes them attractive tools for therapeutic interventions of diseases like cancer, neurodegeneration as well as viral infections.

Carsten Janke leads a research team at the

Institut Curie, Paris. His talk on "Regulation of microtubule functions by posttranslational modifications" summarized his recent discoveries in this rapidly growing field. Microtubules are highly dynamic structures composed of alpha- and beta-tubulins, proteins that are conserved throughout evolution and the basis of numerous cellular activities including cell division, cellular organisation, polarity and movement. Microtubule-associated proteins (MAPs) stabilize these structures and mediate interaction with other cellular components like membrane vesicles. From the viral point of view, microtubules are highways for viral particles on their route through the cytoplasm. Dynamic instability and functional diversity of microtubules could be achieved by a range of posttranslational modifications of its subunits including polyglutamylation glycylation, detyrosination and acetylation. Some of these modifications are reversible, however until recently the enzymatic machinery in particular for their reversion remained unknown. Work in the Janke lab has unveiled several members of the cytosolic carboxypeptidase (CCP) family. Some CCPs shorten polyglutamate chains or remove branching glutamates on tubulin, activities that may strongly influence interaction, stability, and function of microtubules. Strikingly, mouse strains lacking functional CCP1 are prone to degeneration of Purkinje cells supporting a role of CCPs in neurodegeneration.

Thomas Sternsdorf, who is working at the Forschungsinstitut Kinderkrebs-Zentrum at the University Hospital in Hamburg is a longstanding expert in the field of SUMO modifications of proteins. He presented an overview over the field entitled "SUMO: small ubiquitin-like, but different". Both Ubiquitin and SUMO (Small Ubiquitin-like MOdifier) are posttranslationally conjugated to proteins changing their biological properties. While ubiquitylation has a well-described role affecting protein stability and intracellular sorting of the conjugates, the functional consequences of SUMOylation are only beginning to be understood. In his presentation Thomas Sternsdorf described the repertoire of SUMO conjugating enzymes accentuating the role of PML intranuclear bodies as potential sites where SUMO modification might take place under physiological conditions. He presented several new technical approaches that allow studying SUMO-modifications in cell based assays. These techniques included the use of in vitro semi-permeabilized or partially extracted cells (for in-tube assays) functionally preserving PML nuclear bodies and other cellular structures. The addition to such systems of bacterially expressed and purified substrates, of SUMO itself and an energy regenerating system was sufficient to restore SUMOylation indicating that the cellular structures provided the modifying machinery.

Contributions by young scientists

Aside from the invited plenary speakers, this workshop aimed to encourage the participation of young (and not so young) scientists from the field of virology by giving them the opportunity to present their work in the form of 20-minute oral presentations. Like last year, many participants came from outside of Germany underlining the quality of the research presented at and the dynamic nature of this workshop. These talks spanned a wide range of viral systems including alpha- beta and gamma-herpesviruses (HSV, HCMV, EBV), other DNA viruses (adenovirus, papilloma virus) as well as hepatitis virus B and C, influenza virus and some more exotic candidates. The presented topics covered all aspects from virus structure, entry mechanisms, replication, transcriptional control of viral and cellular genes during infections to virus assembly and egress. This wide range of topics stimulated considerable discussion involving several refreshing non-expert contributions of our invited plenary speakers, which gave rise to a new view of these topics, thus perfectly matching the scope of the workshop. These discussions did not stop in the sessions, but continued during, and particularly following, the wine tasting that ended in a social evening accompanied by the excellent food of the Ketschauer Hof.

It was clear from the talks that several state-of-the art technologies have found their place in virus research that is focused around cell biological questions. In several sessions cutting-edge imaging data were presented, such as tomography and live cell imaging. For example, the use of single or dually tagged viruses, genetically modified with GFP and/or mCherry, and approaches using direct labelling with Alexa dyes of non-enveloped viruses was presented. The topics using imaging ranged from attachment, fusion and intracellular transport to virus induced membrane damage, morphogenesis and egress. This was an impressive demonstration how efficiently viruses can be used to highlight processes in living cells or at very high resolution. Others showed the use of cell based assays to reconstitute intracellular processes like virus docking and virus genome release using purified components in semi-permeabilized cells. This was followed by several talks on mechanisms related to viral and cellular gene expression, emphasizing the role of transcriptional and post-transcriptional control of viral and cellular genes as well as immune evasion strategies involving the modification of gene expression. Another group of talks encompassed more global approaches in form of large screening assays or transcription profiling approaches of viral or cellular miRNAs to identify novel restriction mechanisms of virus infections, but also to screen for nucleo-cytoplasmic transport signals. A lot of emphasis was also put on the use of primary cells showing a trend to use physiologically more relevant systems in viral research.

Lastly, as a new idea for this year's workshop, we selected three young scientists who gave excellent presentations, Sabrina Schreiner ("Control of adenoviral gene expression", Heinrich-Pette-Institut, Hamburg), Diana Lieber ("Host miRNA profiling in alpha-herpesvirus replication", Max von Pettenkofer Institute, Munich) and Martin Strehle ("Expression

analysis of MHV68 miRNAs", Helmholtz Centre, Munich). Among these three candidates, Diana Lieber was chosen (based on a random selection between the three candidates) to represent the workshop in an invited talk at the annual meeting of the GfV held in Essen earlier this year.

Workshop 2012: "Nuclear structures and chromatin dynamics"

This year´s workshop will take place September 19th to 21st 2012 at the **Ketschauer Hof** in **Deidesheim** and is entitled "Nuclear structures and chromatin dynamics". Generally, virally encoded proteins and RNAs often dramatically reprogram host gene expression while taking advantage of the host machinery for their own gene expression. Viruses that start their morphogenesis in the host nucleus annex this space for their propagation thereby restructuring the host chromatin. Despite these dramatic consequences for the host, surprisingly little is known how viruses achieve them. Recently, nuclear dynamics in viral infection, a field neglected for a long time, has attracted a lot of attention. To further boost research on this growing field and gain access to the state-of-the-art methodology, we invited three cell biologists specialized on various aspects of this year´s topic to give keynote lectures:

Gernot Längst is professor at the University of Regensburg. His research analyses how genomic DNA is highly compacted and organized into chromatin, while at the same time access of proteins involved in various DNA associated nuclear activities is guaranteed. Using biochemical methods, live cell imaging and deep sequencing the Längst lab analyses how various proteins and non-coding RNAs dynamically regulate chromatin compaction. With his keynote lecture "From local to global chromatin structures - Regulation by chromatin remodeling enzymes and non-coding RNA" Gernot Längst will provide insight into this fascinating research area.

The research of **Cristina Cardoso**, professor at the TU Darmstadt, aims at elucidating principles that enable and govern the dynamic organization of the cell nucleus. To analyse how the genetic and epigenetic information of the genome is replicated in a faithful and coordinated manner her laboratory applies high-resolution microscopy using fluorescent fusion proteins as well as other biochemical and biophysical approaches. Her talk on "DNA replication and repair, a 4D matter" will summarize work of her laboratory that has consequences for genome stability and cancer development, as well as cell differentiation.

Peter Hemmerich, professor at the FLI-Leibniz Jena, analyses structure and function of the cell nucleus with a particular focus on age-related alterations. He aims to determine dynamics and interactions as well as biophysical properties of proteins in their natural environment. To this end he applies high resolution and live microscopy in combination with several other techniques like photobleaching

and -activation, and fluorescence correlation spectroscopy. In his talk entitled "Assessing protein dynamics in the nucleus: new clues on genome function" he will provide insight into the recent development in the field of nuclear dynamics and architecture.

Most importantly, we are very happy to welcome **Prof. Harald zur Hausen** who was awarded the nobel prize for physiology or medicine in 2008 for his life-long research on papillomavirus and their potential to induce cancer. We look forward to host Prof. zur Hausen who will present a lecture of honor.

We would now like to invite researchers of the Cell biology and Virology fields at all levels of their career to join us in Deidesheim and to provide fascinating contributions and to engage in lively discussions.

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Details for the workshop can be obtained at the website of the GfV or by directly contacting the organizers.
http://www.g-f-v.org/inhalt_en.php?lmnop=1&modul=TERMINE&aktion=DETAILS&id=248