L-19
UNDERSTANDING THE MOLECULAR MECHANISMS OF VIRUSES AND HOST INTERACTIONS

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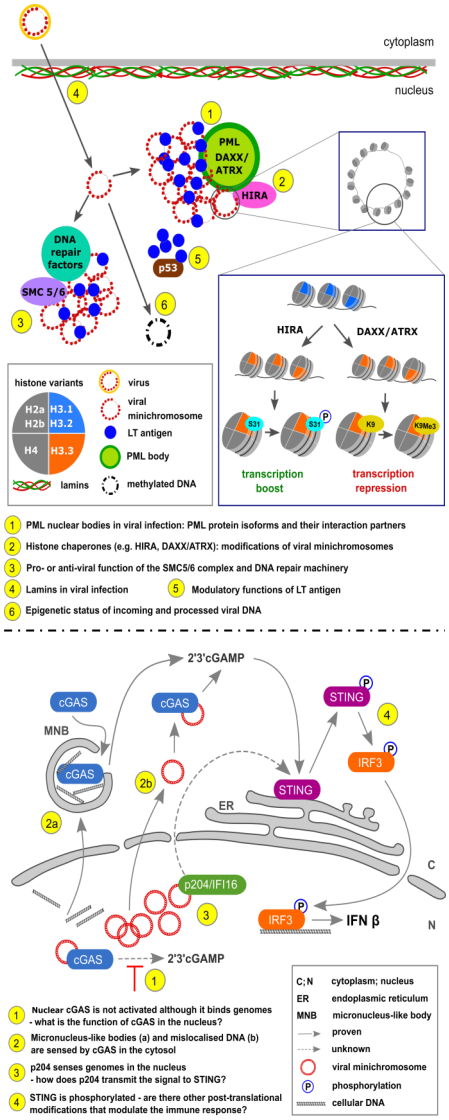
Our research is focused on two objectives, first, the study of interactions between nuclear proteins and viral components which could result in the restriction or establishment of the infection, and second, the elucidation of the mechanisms of innate immune response modulation in infected cells. For that, the model – Murine polyomaviruses (MPyV) and the human pathogen – BK polyomavirus (BKPyV) [1] are used in our lab.

In the first part, we are studying i) the role of PML protein isoforms in viral transcription; ii) the participation of PML-associated chaperons, the HIRA protein, and the DAXX/ATRXX in polyomavirus minichromosomes remodeling and regulation of expression iii) functions of the SMC5/6 protein complex in MPyV replication; iv) role of nuclear lamins in viral infection; v) possible new cell partners of the major viral regulatory protein, LT antigen (this part of the research is carried out in cooperation with Pichová's group from Institute or organic chemistry), and finally, vi) epigenetic modifications of the BKPyV genomes (isolated from patients) that could be connected with transcriptional repression (this work will be performed in cooperation with Stanton's group from Cardiff University, GB, – and Tachezy's group from Charles University). Furthermore, our group will support the studies of validation of the role of PML bodies and the dynamic of HBV DNA chromatinization in the induction of antiviral state in HBV-infected hepatocytes carried out by the group of Šašková, Charles University (our group will perform the standardization of protocols for in-situ DNA hybridization and confocal and super-resolution microscopy studies).

In the second part, we are studying i) the DNA sensors and adaptors involved in the immune sensing of BKPyV in the microvascular endothelial cells which are possible reservoir cells for the virus ii) the mechanisms of activation of the canonical and possibly non-canonical pathways leading to the production of interferon and pro-inflammatory cytokines in BKPyV and MPyV infected cells. For the studies of non-canonical pathways, we focused on understanding the possible activation of STING via TRAF62,3 iii) the mechanisms of modulation of the innate immune responses during MPyV and BKPyV infection by post-translational modification of cGAS DNA sensor and adaptor protein, STING and iv) cross-talk of cell innate immunity and viral components by exploring the interaction between virus early antigens and DNA sensors and adaptors). Furthermore, our group will cooperate with the group of Šašková- Charles University, on studies of the role of plasmacytoid dendritic cells (pDC) in the response to BKPyV. The proposed research is summarized in Scheme 1.



Scheme 1. **Summary of the research topics. The top figure-presents the topics of research for objective 1 and the bottom figure introduces the current model for MPyV immune sensing and the questions that are still unresolved.**

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