INTERACTOME ANALYSIS OF THE MOUSE POLYOMAVIRUS LARGE T ANTIGEN

KAROLÍNA ŠTAFLOVÁ[b], VOJTĚCH ŠROLLER[a]*, IVA PICHOVÁ, JANA BÁRTOVÁ, BORIS RJABČENKO, JITKA FORSTOVÁ and SANDRA HUERFANO

[a] Department of Genetics and Microbiology, Faculty of Science, BIOCEV, Charles University, Vestec 25250, Czech Republic
vojtech.sroller@natur.cuni.cz
[b] Department of Biochemistry, Institute of Organic Chemistry of the Czech Academy of Scineces, Prague 160 00, Czech Republic

Polyomaviruses are small nonenveloped viruses that replicate in the nucleus of the host cell. The mouse polyomavirus (MPyV) large T antigen (LT) is the multifunctional protein expressed in the early phase of the viral infection. LT initiates viral replication, acts as an ATPase, helicase and transactivates late viral expression[1]. Polyomavirus LTs have been shown to interact with a number of cellular proteins such as the oncosuppressor pRB or p53. The interaction of cellular proteins with LT and other early viral antigens leads to reprogramming of the cell, its immortalization and transformation. The LT antigen causes genomic instability of the cell, activates DNA repair mechanisms and prolongs the cellular S-phase. This allows the virus to use host replication proteins for its own use [2]. Due to the multifunctional nature of the LT antigen, it is likely that not all LT interaction partners of mouse polyomavirus are known.

We performed screening of interaction partners of LT in mouse fibroblasts transfected with LT-expressing plasmid using mass spectrophotomether analysis. Selected hits were then confirmed in mouse fibroblasts infected with MPyV by using confical microscopy. We found co-localization of LT and several candidate interacting proteins, namely BAF57, Bag-2, MKK3, PCR1 and WDR48. We focused on the kinase MKK3, which is part of the p38 MAP kinase pathway. However, redusing of MKK3 expression by siRNA had no effect on the number of cells infected with MPyV or the amount of infectious progeny in vitro.

Since the members of the polyomaviridae family share most functional domains, studies of the interaction between the LT of the human Merkel cell polyomavirus and human BK polyomavirus and the proteins selected above will be investigated.

Acknowledgement
The work was supported by the project National Institute of Virology and Bacteriology (Programme EXCELES, ID Project No. LX22NPO5103) – Funded by the European Union – NextGenerationEU.

REFERENCES

1. Campbell, K.S., Mullane, K.P., Aksoy, I.A., Stubdal, H., Zalvide, J., Pipas, J.M., et al.: Genes Dev 11: 1098 (1997).
2. Jiang, M., Zhao, L., Gamez, M., and Imperiale, M.J.: PLoS Pathog 8: e1002898 (2012).