Abstract:

The replication cycle of polyomaviruses is, consistently with other viruses, fully dependent on host cells. Not only the cellular replicational and translational mechanisms are important for viruses, but also the virus infection is affected by other cellular proteins. This work is focused on the role of major cytoplasmic deacetylase, histone deacetylase 6 (HDAC6) in replication cycle of murine polyomavirus (MPyV). We showed that the presence of fully functional HDAC6 is essential for successful and productive infection. We found that HDAC6 affects not only early phase, but also late phase of infection. Cells with inhibited, or absent HDAC6 are infected with decreased effectivity and moreover lower amount of infectious viral particles is produced. On the other side, using cells with partially functional HDAC6, either in its deacetylase activity or in ubiquitin-binding activity, leads to increased ability of MPyV to infect those cells. Analysis of levels of early LT antigen and late structural protein VP1 in the infected cells showed, that viral proteins are affected by HDAC6. Our data suggest, that in the replication cycle of MPyV mainly the ubiquitin-binding domain of HDAC6 is required and the role of this domain in protein metabolism and degradation.

In the second part of diploma project, we constructed expression plasmids carrying early region of murine polyomavirus and human BK polyomavirus, where the tumorigenic antigens are coded. Furthermore, by using CRISPR/Cas9 system we managed to prepare line of human retinal cells RPTEC/hTERT1 with HDAC6 knockout. The detailed characterisation of this cell line is required. After it is done, our cell line and plasmid constructs can be used for research on the role of HDAC6 in polyomavirus induced cell transformation.

Key words: histone deacetylase 6, HDAC6, polyomavirus, replication cycle, viral proteins, deacetylation