P-44
MOUSE PML PROTEIN ISOFORMS AND THEIR ROLE IN MOUSE POLYOMAVIRUS INFECTION

KAROLÍNA ANDEROVÁ*, BORIS RYABCHENKO, VOJTĚCH ŠROLLER, LENKA HORNÍKOVÁ, JITKA FORSTOVÁ, SANDRA HUERFANO*

[a] *Department of Genetics and Microbiology, Faculty of Science, Charles University, BIOCEV, Průmyslová 595, 25250 Vestec, Czech Republic*
karolina.anderova@natur.cuni.cz

Promyelocytic leukaemia nuclear bodies (PML NBs) are dynamic, spherical, membrane-less structures composed of the main scaffold PML protein and a variety of stable or transient partner proteins. Apart from many endogenous functions, PML NBs play an important role in antiviral defence, both as direct restriction factors and as regulators of the interferon responses. Hence, many viruses developed effective mechanisms to counteract this restriction[1–3]. This project uses Mouse polyomavirus (MPyV) as a model for studying interactions of PML and viral components. The mouse PML (mPML) protein occurs in three confirmed (mPML1-3) and six predicted (mPMLX1-X6) isoforms. Individual isoforms may affect the composition and functions of PML NBs and mediate antiviral effects[3]. Our data showed, that during MPyV infection, mPML NBs appeared in close proximity to viral replication centres. In *Pml* KO cells, the transcription of MPyV regulatory genes was significantly increased and the amount of viral progeny was approximately two times higher. These results indicate a potential restriction function of mPML NBs and/or mPML protein in MPyV infection. Therefore, here we focused on the role of the individual mPML isoforms. Their expression has been examined in different mouse tissues – liver, spleen, kidney, lung, heart, femoral muscle, brain and thymus and the detected isoforms have been subsequently tested for PML NBs formation. The expression of all, confirmed and predicted isoforms was proved and, in addition, a novel isoform (named by us mPMLXK) was detected in all tested samples. All confirmed mPML1, mPML2 and mPML3 isoforms formed speckles when expressed in *Pml* KO cells and in WT cells, they incorporated into endogenous mPML NBs. The activity of individual isoforms in IFN signalling and their proposed antiviral role are currently under investigation.

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