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ROLE OF THE PML NUCLEAR BODIES AND ITS ASSOCIATED HISTONES CHAPERONES IN THE REMODELING OG MOUSE POLYOMAVIRUS MINICHROMOSOMES

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Polyomaviruses (PyVs) are small non-enveloped viruses replicating in the host cell nucleus. Viral replication centers (VRCs) share features with cellular euchromatic or heterochromatic regions, depending on the stage of infection. In the mouse polyomavirus (MPyV) virions, the circular dsDNA genome and cellular histones are present in the form of a condensed minichromosome arranged into 24 nucleosomes. Here we studied the contribution of PML NBs and their chaperone complexes HIRA and ATRX/DAXX in remodeling MPyV chromatin.

We demonstrated that, in addition to canonical histones, PyV minichromosome contains the non-canonical histone, H3.3, Accumulation of H3.3 in VRCs occurs as early as 24 hours post infection (hpi) when viral genomes undergo massive replication. Furthermore, we showed that PML NBs surround VRCs and increase in number and size as the infection progresses. The proximity of PML NBs to VRCs is retained even after inhibition of viral DNA replication which indicates that PML NBs could directly recognize viral chromatin. Next, although we found that DAXX and ATRX, appear in the VRCs 24 hpi, the absence of DAXX did not prevent H3.3 incorporation into virions, suggesting that other chaperones, e.g. HIRA contribute to the deposition of the H3.3.

Surprisingly, we observed that knockout of *PML* gene leads to increased accumulation of H3.3 in viral minichromosomes and is beneficial for viral transcription. Thus, the PML NBs limit or 'buffer' the accumulation of H3.3 in PyV minichromosomes.

Our results highlight the possibility that HIRA is the chaperone responsible for H3.3 deposition into MPyV genomes and its function is controled by PML NBs. Next, this hypothesis will be investigated. Furthermore, the distribution of H.3.3 in the genomes, its post-translational modifications and the impact of H.3.3 in the transcription of genomes will be studied.

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