Scientific session:

Nuclear Compartments and Gene Expression

Title:

The H3.3 histone variant and its chaperones in polyomaviral infection.

List of authors:

Ryabchenko B, Satratzemis C, Forstová J and Huerfano S.

Abstract text:

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 virion, the circular dsDNA genome and cellular histones are present in the form of a condensed minichromosome arranged into 24 nucleosomes. In this study, we demonstrate 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. The DAXX (death domain-associated) and ATRX (6-alpha-thalassemia, mental retardation X-linked syndrome) proteins, which form a histone chaperone complex that resides in PML NBs (promyelocytic leukemia nuclear bodies), appear in the VRCs 24 hpi, but, in the late phase of infection (when heterochromatinization of viral genomes and assembly of virions take place), only DAXX without ATRX is located in the VRCs. 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 replication which indicates that PML NBs could directly recognize viral chromatin. Knockout of *Pml* or *Daxx* gene leads to increased accumulation of H3.3 in viral minichromosomes. Moreover, knockout of *Pml* gene is beneficial for PyV transcription. We suggest that PML NBs limit the accumulation of H3.3 into viral minichromosomes, and that also other histone chaperones than DAXX-ATRX (e.g., HIRA) are involved in PyV minichromosome modification. The ATRX-independent localization of DAXX in the VRCs during the late stage of infection suggests a yet unidentified function of the protein. The level of transcription of H3.3-deficient PyV, the distribution of H3.3 within the PyV minichromosomes and its post-translational modifications will be the subject of future research.

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