How incoming adenoviruses change their chromatin structure for efficient gene expression

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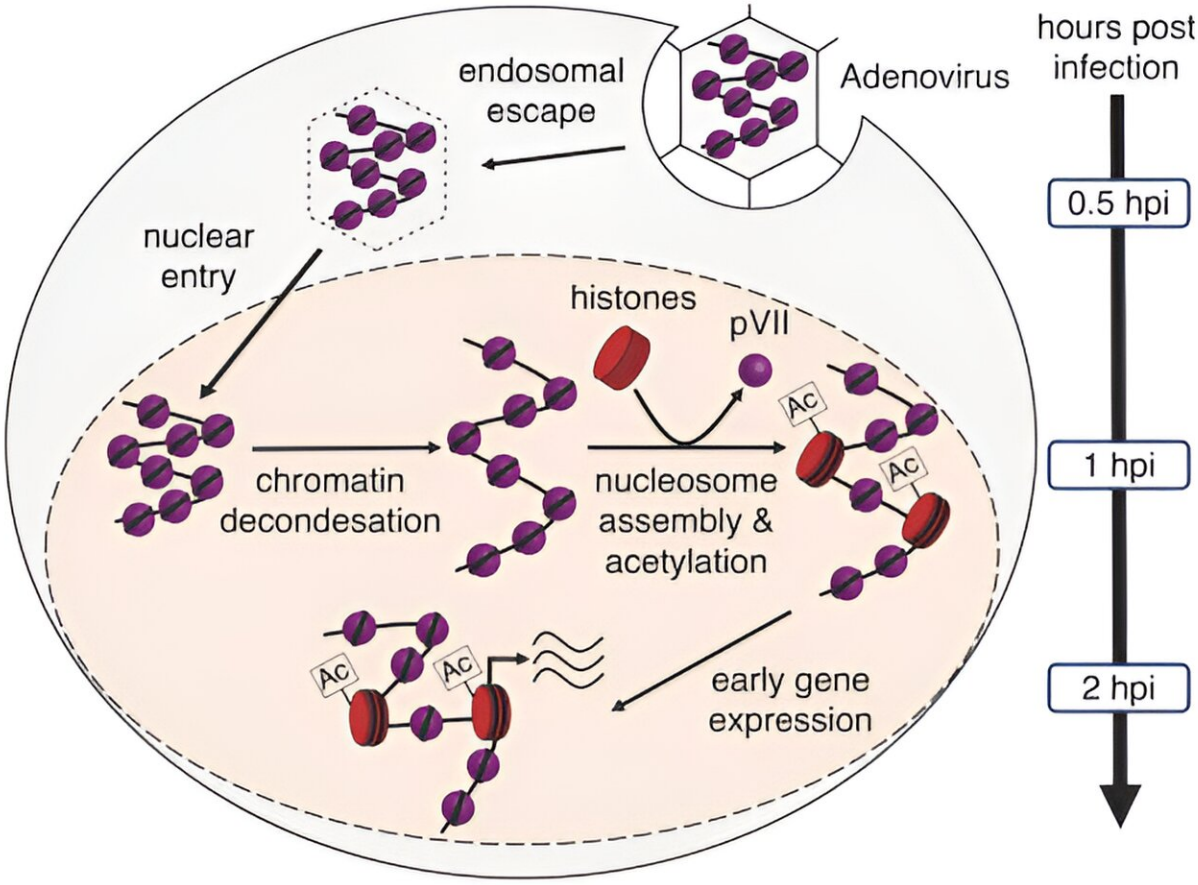

Adenovirus DNA is packaged by the adenoviral nucleoprotein pVII in a chromatin-like manner. Here, exploration of the adenoviral chromatin structure and dynamics during early infection reveals replacement of the pVII protein by host nucleosomes at early gene loci prior to transcriptional activation. Credit: *The EMBO Journal* (2023). DOI: 10.15252/embj.2023114162

Adenoviruses, known for their low pathogenicity and technological approachability, have become instrumental in many therapeutic applications, including as a vaccination vector platform during the recent SARS-CoV-2 pandemic. Central to their efficacy is their remarkably efficient delivery and expression of their genetic material.

Two scientific teams led by Gernot Laengst from the University of Regensburg and Harald Wodrich from the University of Bordeaux have obtained insight into this process in unprecedented detail. Employing advanced microscopy techniques and genome structure analyses, they traced the early stages of adenoviral infection in human cells. The study was recently published in the *EMBO Journal*.

This approach allowed a detailed description of the viral genome intricately wrapped with the viral pVII protein within the incoming virion. Furthermore, their investigation revealed the transformation of the viral chromatin structure, converting the densely packed genome into an exceptionally efficient template for gene expression as it traverses from the cell surface to the cell nucleus.

The scientist could show that in the virus, the viral DNA is tightly wrapped around the viral pVII protein. This unique conformation facilitates seamless accommodation of the genome within the confined viral capsid. Once viruses enter the cell, the packaged viral DNA completes its journey to the nucleus in approximately 30 minutes.

Following capsid release and nuclear import, parts of the viral genome alter the transport configuration and open up. During this process, a few pVII proteins are specifically removed and replaced by cellular histone proteins at the regulatory sites of early activated viral genes.

This strategic exchange with histone proteins unlocks the potential for the viral genetic information to hijack the cellular transcription machinery, enabling efficient gene expression—a process that starts around 30 minutes after the genome arrives in the nucleus, culminating in cell infection.

By comprehending the intricate structural dynamics of the adenoviral genome during the initial stages of infection, the researchers aim to leverage this knowledge for the enhancement of adenoviral vector design. This holds promise for refining applications such as vaccination and gene therapy, thereby elevating both safety and efficiency.

More information: Uwe Schwartz et al, Changes in adenoviral chromatin organization precede early gene activation upon infection, *The EMBO Journal* (2023). DOI: 10.15252/embj.2023114162

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