Scientists advance understanding of herpesvirus infection

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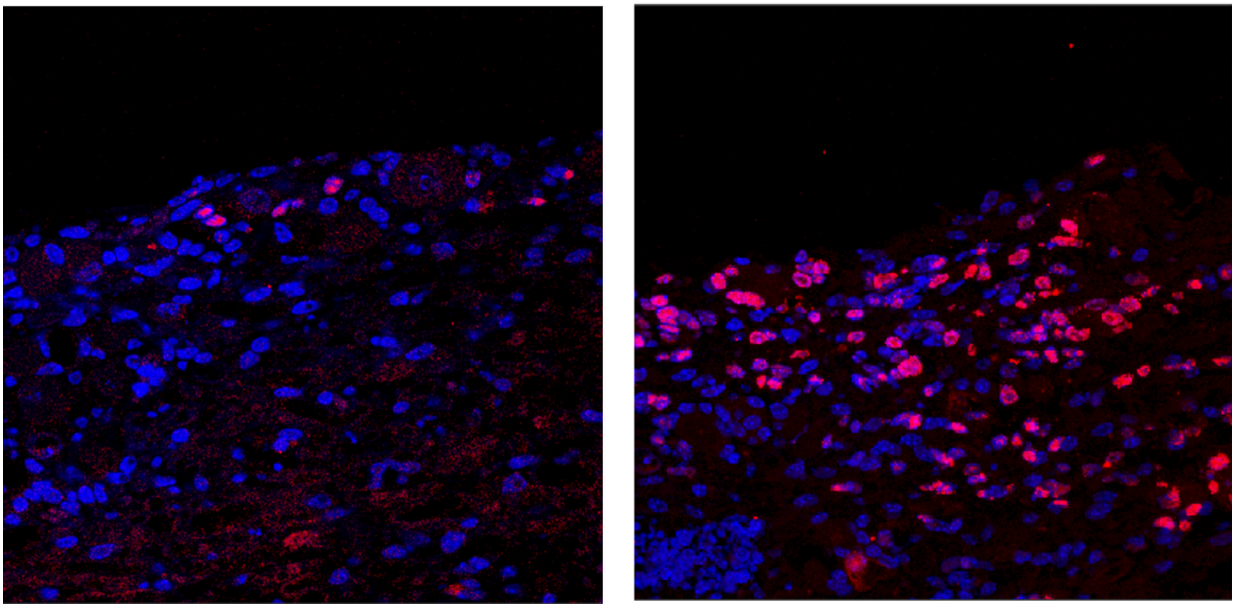

The left image shows typical HSV reactivation (red) from latency in neurons. On the right, viral reactivation is stimulated by compounds that activate the HCF-1 binding partners. Credit: NIAID

Herpes simplex virus (HSV) infections last a lifetime. Once a person has been infected, the virus can remain dormant (latent) for years before periodically reactivating to cause recurrent disease. This poorly understood cycle has frustrated scientists for years. Now, National Institutes of Health (NIH) scientists have identified a set of protein complexes that are recruited to viral genes and stimulate both initial

infection and reactivation from latency. Environmental stresses known to regulate these proteins also induce reactivation.

Globally, the World Health Organization estimates that one-half billion people are infected with HSV-2 while two-thirds of the population are infected with HSV-1. These viruses cause human diseases ranging from oral cold sores to genital lesions to serious eye conditions that can lead to blindness. In infants, HSV can cause neurological and developmental problems. People infected with HSV also have an enhanced risk of acquiring or transmitting human immunodeficiency virus (HIV).

Scientists at NIH's National Institute of Allergy and Infectious Diseases previously made progress toward understanding the role of cellular protein HCF-1 in initiating HSV infection and reactivation. HCF-1 and associated proteins are recruited to the viral genome to enable the virus to replicate and spread. This previous work identified targets for the development of therapeutics to suppress infection and reactivation.

Their latest work, with collaborators from Princeton University, identifies new HCF-1 protein complexes that play additional roles in initiating viral infection and reactivation. The scientists found they could reactivate latent HSV in a mouse model using compounds that turn on components of these HCF-1 protein complexes. Interestingly, some of these HCF-1-associated proteins also are involved in HIV reactivation from latency.

The researchers are continuing to investigate the protein complexes involved in promoting HSV gene expression, infection, and reactivation from latency. Identifying these complexes and understanding the mechanisms by which they function can potentially reveal additional targets for the development of new therapeutics.

More information: Roberto Alfonso-Dunn et al, Transcriptional

Elongation of HSV Immediate Early Genes by the Super Elongation Complex Drives Lytic Infection and Reactivation from Latency, *Cell Host & Microbe* (2017). DOI: 10.1016/j.chom.2017.03.007