Herpesvirus study in mice leads to discovery of potential broad-spectrum antiviral

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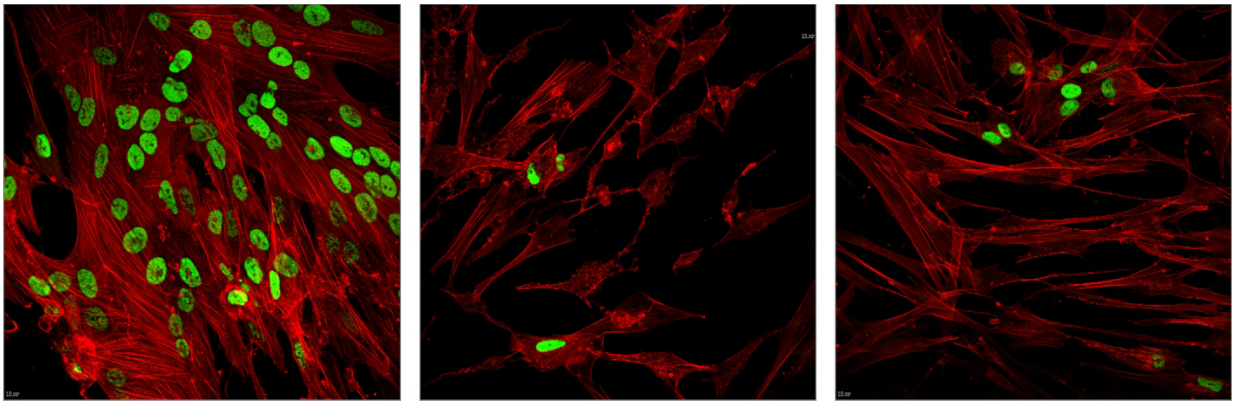

The spread of herpes simplex virus infection (green, left) is suppressed in cells treated with EZH2/1 inhibitors (GSK126 or GSK343). Credit: NIAID

After herpesviruses infect a cell, their genomes are assembled into specialized protein structures called nucelosomes. Many cellular enzyme complexes can modulate these structures to either promote or inhibit the progression of infection. Scientists studying how one of these complexes (EZH2/1) regulated herpes simplex virus (HSV) infection unexpectedly found that inhibiting EZH2/1 suppressed viral infection. The research group, from the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health, then demonstrated that EZH2/1 inhibitors also enhanced the cellular antiviral response in cultured cells and in mice.

Once a person has been infected with a herpesvirus, the virus persists in a latent form, sometimes reactivating to cause recurrent disease. Two-thirds of the global population are infected with HSV-1, and at least 500 million are infected with HSV-2, according to the World Health Organization. These viruses cause a range of diseases and conditions from oral cold sores to genital lesions to serious eye infections that can lead to blindness. In infants who acquire the infection from their mothers, HSV can cause neurological and developmental problems. People infected with HSV also have an enhanced risk of acquiring or transmitting human immunodeficiency virus (HIV). Treatment usually involves antiviral drugs that interfere with viral replication, but new approaches to combat these infections are needed.

The NIAID group demonstrated that EZH2/1 inhibitors not only suppressed HSV infection, spread, and reactivation in mice, but also suppressed human cytomegalovirus, adenovirus, and Zika virus infections in cell culture using human primary fibroblast cell lines. These authors suggest that EZH2/1 inhibitors have considerable potential as broad-spectrum antivirals.

More information: J. Arbuckle, et al. Inhibitors of the histone methyltransferases EZH2/1 induce a potent antiviral state and suppress infection by diverse viral pathogens. *mBio*. DOI: 10.1128/mBio.01141-17 (2017).

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