Abstract

A Genome-Wide CRISPR Activation Screen Identifies Genes Involved in Protection from Zika Virus Infection

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Abstract: Zika virus (ZIKV) is an arthropod-borne emerging pathogen causing febrile illness. ZIKV is associated with the Guillain-Barré syndrome and other neurological complications. The vertical transmission of ZIKV can cause fetus demise, stillbirths or severe congenital abnormalities and neurological complications. There is still no vaccine or specific treatment for ZIKV infection. To identify the host factors that can rescue cells from ZIKV infection, we used a genome-scale CRISPR activation screen. Our highly ranking hits included a short list of interferon-stimulated genes (ISGs) previously reported to have antiviral activity. Validation of the screen results highlighted interferon lambda 2 (*IFN-lambda2*) and interferon alpha-inducible protein 6 (*IFI6*) as genes providing high levels of protection from ZIKV infection. The activation of these genes had an effect at an early stage in the viral infection. In addition, infected cells expressing single guide RNAs (sgRNAs) for both of these genes displayed lower levels of cell death than did the controls. Furthermore, the identified genes were significantly induced in ZIKV-infected placenta explants. These results highlighted a set of ISGs directly relevant for rescuing cells from ZIKV infection or its associated cell death, thus substantiating CRISPR activation screens as a valid tool for identifying host factors impeding pathogen infection.

Keywords: Zika virus; CRISPR screen; interferon-stimulated genes

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