

## Abstract

# SAMHD1 Enhances Chikungunya and Zika Virus Replication in Human Skin Fibroblasts <sup>†</sup>

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<sup>†</sup> Presented at Viruses 2020—Novel Concepts in Virology, Barcelona, Spain, 5–7 February 2020.

Published: 17 June 2020

**Abstract:** Chikungunya virus (CHIKV) and Zika virus (ZIKV) are emerging arboviruses that pose a worldwide threat to human health. Currently, neither vaccine nor antiviral treatment to control their infections is available. As the skin is a major viral entry site for arboviruses in the human host, we determined the global proteomic profile of CHIKV and ZIKV infections in human skin fibroblasts using stable isotope labelling by amino acids in cell culture (SILAC)-based mass spectrometry analysis. We show that the expressions of the interferon-stimulated proteins MX1, IFIT1, IFIT3 and ISG15, as well as expressions of defense response proteins DDX58, STAT1, OAS3, EIF2AK2, and SAMHD1 were significantly upregulated in these cells upon infection with either virus. Exogenous expression of IFITs proteins markedly inhibited CHIKV and ZIKV replication which, accordingly, was restored following the abrogation of IFIT1 or IFIT3. Overexpression of SAMHD1 in cutaneous cells or pretreatment of cells with the virus-like particles containing SAMHD1 restriction factor Vpx resulted in a strong increase or inhibition, respectively, in both CHIKV and ZIKV replication. Moreover, silencing of SAMHD1 by specific SAMHD1-siRNA resulted in a marked decrease in viral RNA levels. Together, these results suggest that IFITs are involved in the restriction of replication of CHIKV and ZIKV and provide, as yet unreported, evidence for a proviral role of SAMHD1 in arbovirus infection of human skin cells.

**Keywords:** Chikungunya virus (CHIKV); Zika virus (ZIKV); SAMHD1



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