Host Cell Factors and Modulation

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Phospholipid Scramblase 1 regulates viral gene expression of Herpes simplex virus Type 1

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Phospholipid scramblase 1 (PLSCR 1) is a membrane-associated protein conserved in all eukaryotic cells. Initially identified as a component involved in redistribution of phospholipids between plasma-membrane bilayers, PLSCR1 may have additional functions in signalling, apoptosis, cell proliferation, and transcription. Moreover, PLSCR1 modulates viral infectivity as reported for Vesicular stomatitis virus (VSV), Human Immunodeficiency Virus (HIV), and Hepatitis C Virus (HCV).
Herpes simplex virus 1 (HSV-1), a large enveloped DNA virus, is a human pathogen that causes latent infections in sensory neurons. To explore a role of PLSCR1 during HSV-1 infection, RNAi was applied on HeLa cells followed by HSV-1 infection. PLSCR1 specific siRNAs effectively depleted the PLSCR1 protein while cell viability remained unaffected. In absence of PLSCR1, docking and entry of HSV-1 virus particles into host cells appeared normal. In contrast, expression of several viral genes was strongly diminished as determined both on the transcript and protein level. Interestingly, while transcripts of various kinetic classes were reduced, expression of ICP27 as well as cellular genes was comparable in PLSCR1-depleted and control cells. Unsurprisingly, viral replication was significantly reduced by 1-2 logs. While HSV-1 particles were formed, extracellular virions released by PLSCR1-depleted cells showed an increased genome copy/pfu ratio in line with their reduced infectivity. Together our data support a positive impact of PLSCR1 on HSV-1 infection that potentially occurs on multiple levels making PLSCR1 a novel target of antiviral therapy.

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