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Differential impact of SEC61B on the processing and function of filovirus glycoproteins

Inhalt

Current antiviral drugs mainly target viral proteins, resulting in resistance development and the need for new antivirals. In particularly, broad-spectrum are urgently needed to combat zoonotic spillover events. Generating host-directed antivirals may constitute a strategy to combat both issues and endoplasmic reticulum (ER) proteins may represent suitable targets. We assessed the potential of the ER translocation channel SEC61 as a therapeutic target. For this, we created cell lines with a knockout (KO) of SEC61B, a subunit of the SEC61 channel, and examined the effects on processing and function of glycoproteins (GPs) of zoonotic viruses. While SEC61B-KO had no impact on processing of the Ebola virus (EBOV) GP, cleavage of Marburg virus (MARV) GP was abrogated. SEC61B-KO in target cells reduced entry of particles pseudotyped with EBOV-GP while SEC61B-KO in cells producing MARV-GP pseudotypes reduced production of infectious particles. To determine whether SEC61B-KO affects viral replication, we used replication-competent, chimeric vesicular stomatitis virus (VSV) expressing EBOV-GP or MARV-GP. Both chimeric viruses but not VSV showed reduced replication in SEC61B-KO cells and an inhibitor of the SEC61 channel, Apratoxin S4, was more active against VSV-EBOV-GP and VSV-MARV-GP as compared to VSV. Although the mechanism of underlying antiviral activity remains to be fully elucidated, our data suggest that targeting the SEC61 channel may represent a viable antiviral strategy.

Keywords

Filoviruses, Glycoproteins, ER translocation, CRISPR/Cas9

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Yes, I am a Junior Scientist.

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Typ des Beitrags: Both Options Possible