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Abstract

Development of a T7-Independent MARV Minigenome System †

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Abstract: Marburg virus (MARV) is the only known pathogenic filovirus that does not belong to the genus *Ebolavirus*. It causes a severe hemorrhagic fever that is associated with a high mortality rate (>80%). The potential for filoviruses to cause devastating outbreaks, in combination with the lack of licensed therapeutics and vaccines for Marburg virus disease, illustrates the need for more MARV research. However, research involving MARV is hindered by its dependency on access to high-containment laboratories. Virus alternatives such as minigenomes have proven to be a useful tool to study virus replication and transcription at lower biosafety levels, and can be used for antiviral compound screening. All currently available MARV minigenomes are dependent on the addition of an ectopic T7 RNA polymerase that can drive minigenome expression. While this allows for high expression levels, the ectopic expression of a T7 polymerase is not feasible in all cell types, and acts as a confounding factor in compound screening assays. We have developed an alternative MARV minigenome system that is controlled by an RNA polymerase II promoter, which is natively expressed in most mammalian cell types. We show here that this novel minigenome can be used in a wide range of cell types, and can be easily amended to a 96-well format to be used for high-throughput compound screening, thereby providing a valuable alternative to previously developed MARV minigenomes.

Keywords: MARV; Marburg virus; Minigenome; RNA polymerase II