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Replication assessment of chimeric HEV-3 subtypes demonstrates enhanced replication fitness of HEV-3f isolates

Inhalt

Hepatitis E virus (HEV) remains an underestimated global health concern, causing an estimated 20 million infections and 3450 - 70,000 deaths annually. In Europe, genotype 3 (HEV-3) is the prevalent genotype, comprising 15 subtypes organized in three clades: Clade 1 (3efg), Clade 2 (3abchijklmno) & Clade 3 (3ra). Infections with HEV 3 clade 1 have been associated with more severe disease outcomes, although the underlying mechanisms remain unclear.

We performed a phylogenetic analysis of HEV-3 subtypes and generated a library of 15 primary isolate-derived polymerase chimeras, each inserted into the backbone of the Kernow-C1 p6 subgenomic replicon. We evaluated replication kinetics and identified molecular determinants of HEV replication.

Phylogenetic analysis revealed considerable diversity among the HEV-3 polymerases, with up to 21 substitutions relative to p6. 13 of the 15 chimeras demonstrated replication comparable to the parental p6 construct. The HEV-3f subtype showed significantly enhanced replication kinetic, with up to a 5-fold increase after 24 h. Our findings highlight the genomic flexibility of HEV-3, which allows for efficient replication of diverse chimeric constructs. This model provides a robust platform for assessing intra-genotypic variability in antiviral responses and advances our mechanistic understanding of replication fitness. Such insights are critical for optimising treatment strategies and understanding the burden of disease in HEV-infected patients.

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Hepatitis E, HEV, Viral hepatitis

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Yes, I am a Junior Scientist.

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