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A self-recombinant hepatitis E virus derived from a chronically infected patient efficiently replicates in cell culture

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Hepatitis E is an increasingly reported disease in Germany. Studies on the replication cycle of hepatitis E virus (HEV) and development of vaccines are hampered due to the lack of efficient and robust cell culture systems for this virus.
We describe the successful isolation of HEV derived from a chronically infected transplant patient held under immunosuppressive therapy. Inoculation of a serum sample onto the human lung carcinoma cell line A549 resulted in replication of the virus as shown by RT-qPCR. The inoculated HEV strain is closely related to a wild boar-derived genotype 3 strain from Germany; however, this wild boar strain did not replicate in A549 cells. The most obvious difference between both strains was an insertion of 186 nucleotides in the hypervariable region of the patient strain, originating from the HEV ORF1 region. By passaging of the infected cells, a cell line continuously producing HEV particles could be generated as demonstrated by RT-qPCR, electron microscopy and immunohistochemistry. Infectivity of the produced virus was demonstrated by inoculation onto fresh A549 cells and two consecutive passages. The HEV strain derived from the second passage showed several point mutations scattered around the whole genome; however, the insertion was still present.
The data indicate cell culture replication of an uncommon HEV strain. Recently, cell culture isolation of two other HEV strains carrying also insertions in their hypervariable regions, but originating from human ribosomal RNA genes, have been described by other groups. Altogether these findings may indicate that tissue culture adaptation of HEV is mostly dependent on the length and position of the insertion, but only to lesser degree on the sequence itself.

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