

Article

Understanding Hepatitis E Viruses by exploring the structural and functional properties of ORF4

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Abstract

Hepatitis E virus (HEV) belongs to the family *Hepeviridae* and is the major cause of hepatitis E infections across the globe. Recently, a novel viral protein of HEV, named as open reading frame (ORF4), has been associated with its replication in genotype 1 isolates. However, much information regarding ORF4 has not been explored. Thus, the study was conceptualized to explore the structural and functional features of HEV ORF4 protein to better understand the possible molecular mechanisms. The detailed investigation of the ORF4 was carried out in terms of its physicochemical properties, secondary and tertiary structure predictions and functional analysis using different bioinformatics tools. The *in silico* analyses revealed that ORF4 sequences were enriched in Serine, Proline and Glycine amino acid residues suggesting the prevalence of disordered residues. The protein was found to be thermostable, unstable and highly hydrophobic. The structural analysis showed the presence of cleft, tunnel and pore suggesting their participation in interaction with other molecules. Moreover, identification of several modified sites in ORF4 sequences such as glycosylation, phosphorylation and myristoylation sequences suggest their involvement in cellular signaling pathways and biological processes. Thus, taken together, it can be interpreted that HEV ORF4 possesses significant enormous flexibility due to the presence of Serine, Glycine and Proline amino acids, which suggest its involvement in protein-protein interaction. Furthermore, the presence of motifs, clefts and tunnels also strengthens our analysis, suggesting the commitment of ORF4 towards interaction with other target molecules. Thus, it could be potent drug-targets.

Keywords Hepatitis E virus; open reading frame (ORF4); physicochemical parameters; structural analysis; functional analysis.

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1 Introduction

Hepatitis E virus (HEV) is the major aetiological agent of Hepatitis E, also called enteric hepatitis (enteric means related to the intestines) infection (Kumar et al., 2013; Khuroo and Khuroo, 2016). HEV is a

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