



In silico Analysis for Comparative Modeling of ORF-1 Polyprotein Domains of Hepatitis- E Virus

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ABSTRACT : Hepatitis E is a form of liver disease characterized by inflammation of the liver due to infection with the Hepatitis E virus, whose structure is not present in PDB so structure prediction is important to stop the virus in future. The FASTA sequence of the ORF-1 Polyprotein of HEV was retrieved from NCBI (NCBI Reference Sequence: NP_056779.1), which does not show any transmembrane proteins in their structure. The best quality templates were taken from HHpred server. Then with the help of MODELLER, it was generated 3 models which were further refined and validated by using SAVS (Structural analysis and verification server) with validation programme like Procheck for getting the best model with high Ramachandran plot score value. The best model obtained was model_3 (6197496_pdb), which is having a maximum Ramachandran score of 92.2 per cent, of the residues and had an average 3D-ID score > 0.2.

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Hepatitis- E is a viral hepatitis (liver inflammation) caused by infection with a virus called hepatitis E virus (HEV). Hepatitis B virus is a *Hepadnavirus hepa* from *hepatotropic* (attracted to the liver) and *dna* because it is a DNA virus (Panda and Jameel, 1997) and it has a circular genome of partially double-stranded DNA. The viruses replicate through an RNA intermediate form by reverse transcription, which in practice relates them to retroviruses (Locamini, 2004). Although replication takes place in the liver, the virus spreads to the blood where viral proteins and antibodies against them are found in infected people. The life cycle of hepatitis B virus is complex. Hepatitis B is one of a few known pararetro viruses: non-retroviruses that still do use reverse transcription in their replication process. Because the virus multiplies via RNA made by a host enzyme, the viral genomic DNA has to be transferred to the cell nucleus by proteins (Beck and Nassal, 2007). The

genome is approximately 7200 bases in length, is a polyadenylated single-strand RNA molecule that contains three discontinuous and partially overlapping open reading frames (ORFs) along with 5' and 3' cis-acting elements, which have important roles in HEV replication and transcription. ORF1 encodes a methyltransferase, protease, helicase and replicase. ORF2 encodes the capsid protein and ORF3 encodes a protein of undefined function. The ORF-1 of Hepatitis E virus (HEV) encodes a nonstructural polyprotein of ~186 kDa that has putative domains for four enzymes methyltransferase, helicase, protease and replicase (Ansari *et al.*, 2000). In the absence of culture system of HEV, the ORF-1 expressed using bacterial and mammalian expression system has shown an ~186 kDa protein, but no processing of the polyprotein is observed. It was proposed that the ORF-1 polyprotein does not undergo processing into functional units. When expressed in insect cells, ORF1 was processed and this was partially blocked by a cell permeable