

Structural characterization of the Hepatitis C Virus E2 glycoprotein: computational and experimental approaches

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Hepatitis C virus (HCV) infection is a major cause of chronic liver disease worldwide. Although effective therapeutic approaches, based on specific inhibitors of HCV proteins NS3/4A and NS5B, have been recently discovered, their use is limited by the elevated costs of these drugs. Currently, there is neither an effective immune globulin for prophylaxis nor a vaccine for the prevention of hepatitis C. A particularly attracting target is represented by the immunogenic E2 glycoprotein, a key factor for HCV entry in host cells. This protein has been the subject of recent structural studies that have greatly expand our current knowledge of HCV pathogenicity (Khan et al. 2015; Khan et al. 2014; Kong et al. 2013). In this framework, we have recently undertaken studies aimed at evaluating the potential of some regions of the protein as vaccine candidates (Sandomenico et al. 2015, under review). We here investigated the structural/dynamic features of the E2 protein, whose structure has been recently solved by two independent groups in complex with antibodies. Molecular dynamics simulations carried out on the protein core provided interesting information on both global dynamics of the protein and on local features of important regions. Moreover, a combined experimental/computational analysis shows that the epitope I region (residues 412-422) is endowed with an elevated structural versatility. Collectively these findings provide useful information for future studies aimed at designing anti-HCV vaccines.

References

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