Key messages

Human parvovirus B19, a member of the Erythrovirus genus Parvoviridae (Ballou et al., 2003) infects predominantly erythroid precursor cells in human bone marrow and fetal liver tissues and induces cell death to the infected cell directly (Brown et al., 1994).

The B19 genome has two large open reading frames (ORFs), with the single nonstructural (NS1) protein encoded by genes on the left side of the genome and the two capsid proteins (VP1 and VP2) on the right side (Ozawa et al., 1987). Sequence analysis, functional family annotation and proteonomic analysis for VP2 protein reveals its importance in viral capsid formation, pathogenicity and usefulness as a drug target against the viral infection.

Currently there is no vaccine and no specific treatment for parvovirus B19 infection. The initial symptoms can be treated using over counter medications, such as acetaminophen or ibuprofen.

Unavailability of proficient vaccine or drug to combat B19 virus, the availability of whole genome sequence of human parvovirus B19 on open source to discover conserved protective antigens encouraged to follow a Bioinformatics approach to identify a drug target through structure based drug designing.

Material and methods

Through virtual screening ten potential inhibitors targeting VP2 protein of human parvovirus B19 was identified. Telomerase inhibitor (viii) was found as the best probable lead among inhibitor against parvovirus.

Presence of 14 antigenic sites in VP2 protein refers to its high degree of antigenicity and its non homology with human confirmed it as potential drug target for discovery of potent ral drug against parvovirus B19.

The SVM-Prot functional annotation of VP2 protein had shown its Zinc binding, Coat and envelope protein like and Calcium-binding properties. Higher Zinc binding property of the liver proteins (VP1 and VP2) on the right side (Ozawa et al., 1992).  Coat and envelope protein like properties signifies presence of the protein in viral outer membrane.

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Fig.1 : A) Telomerase inhibitor (viii) – human Parvovirus B19 VP2 protein docking complex. B) The docking complex showing VP 2 protein residues blocked by Telomerase inhibitor (viii). Three hydrogen bonds formed were shown in green dotted lines. C) Interacting residues of VP2 protein with Telomerase inhibitor (viii) in Surface view.

Table1: List of antigenic peptides of VP2 protein and ligands

Table2: Summary of docking information of the ten top ranked poses of VP2 protein with ligands (values copied from the table browser window of Discovery studio 2.0).

Results and Discussion

VP2 is the major structural protein, accounting for 96% of total capsid protein. The VP2 protein is encoded by sequences from nucleotides 3125 to 4786, having molecular mass of 58 kDa with 554 amino acid length. The VP2 protein belongs to different protein function families like Zinc-binding (91.3%), Coat protein (68.5%), Outer membrane (58.6%), Chlorophyll biosynthesis (58.6%), DNA repair (58.6%) and Calcium-binding (58.6%). The SVM-Prot functional annotation results had confirmed that VP2 protein is essential for constant parvovirus B19 infection and pathogenicity.

Jembo antigenic server predicted presence of potentially 14 antigenic regions in human parvovirus B19 (Table 1). Presence of 14 antigenic sites in VP2 protein refers to its high degree of pathogenicity.

Homology search against human genome had revealed that VP2 protein was not having significant similarity with host genome. Thus, VP2 protein would be highly useful as molecular target for designing antiviral drug against parvovirus B19 infection.

VP2 protein crystal structure was retrieved from protein data bank (PDB ID 1S58). The VP2 protein crystal structure was imported to Discovery studio visualizer. 22 Binding sites were predicted and largest binding site was expanded to 20Å in x, y and z axis direction from its centroid and used for virtual screening.

The prepare ligand protocol helps to prepare ligands for input into other protocols. Harvard’s ChemBank is the database of Food and Drug Administration approved drugs. The database having 2344 small molecule entries was downloaded. Tautomers and isomers were generated for each ligand conformations with a pH range of 6.5 to 8.5. Duplicate structures were removed, Lipinski’s filter was applied and the 3D binding assays are necessary for confirming the activity of predicted lead molecules.

Conclusion

The SVM-Prot functional annotation of VP2 protein had shown its Zinc binding, Coat and envelope protein like and Calcium-binding properties. Higher Zinc binding property of the protein refers to its critical role in maintaining viral stability (Funk et al., 1992). Coat and envelope protein like properties signifies presence of the protein in viral outer membrane. Calcium ions appear to play a major role in maintaining the structural integrity and are likely involved in the process of viral uncoating (Rebecca et al., 1996).

Presence of 14 antigenic sites in VP2 protein refers to its high degree of antigenicity and its non homology with human confirmed it as potential drug target for discovery of potent inhibitor against parvovirus.

Through virtual screening ten potential inhibitors targeting VP2 protein of human parvovirus was identified. Telomerase inhibitor (viii) was found as the best probable lead among the ten. However, in vitro binding assays are necessary to confirm the inhibition ability of the proposed lead molecules.

Acknowledgements: We are highly thankful to DBT, Ministry of Science and Technology, Govt. of India for financial support. We are grateful to Dr. B. Vengamma, Director, for providing constant support and encouragement for research at Bioinformatics centre.