Functional annotation of human *parvovirus b19* proteome and molecular docking of VP1 protein with teniposide
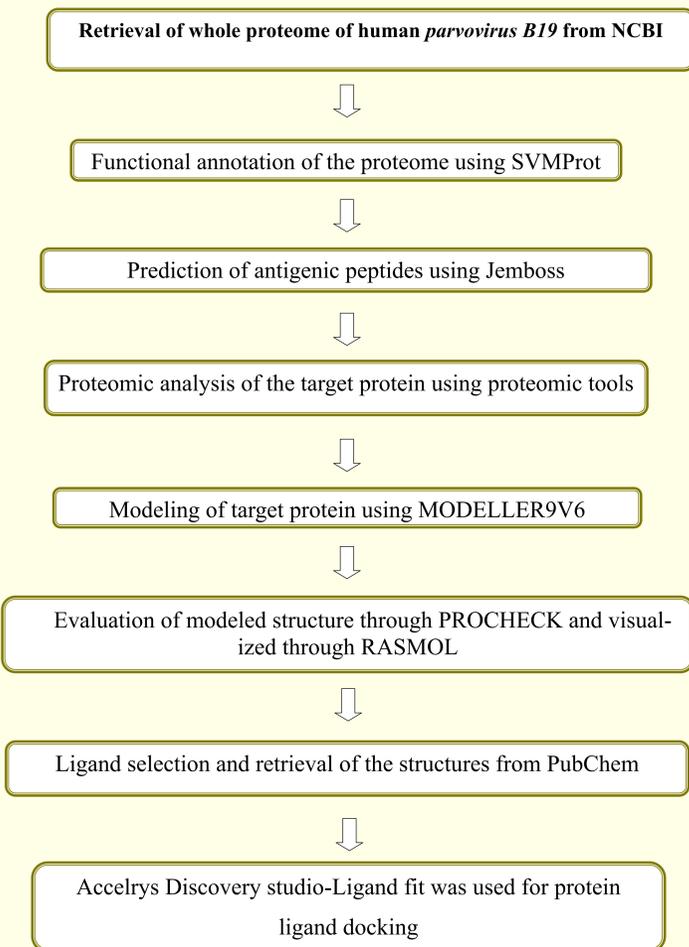
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Key Messages

. Human *Parvovirus B19* is a common source of infection with a seroprevalence of 60-70% in the population. The initial symptoms include headache, body ache, sore throat, mild fever, chills, nausea, pyrexia, coryza and diarrhoea. It causes several distinct clinical syndromes such as erythema, polyarthritis resembling rheumatoid arthritis, vasculitis, hydrops fetalis, myocarditis etc. Transmission of infection occurs via the respiratory route, through blood products administered parenterally and vertically from mother to fetus (Heegaard and Brown, 2002).

. Infections occur globally and are similar in U.S, Europe and Asia. Approximately 50% of children have detectable IgG to *B19* by the age of 15. Infection occurs throughout adult life, so that 80% of the elders are seropositive (Cohen and Buckley, 1988). Women of child-bearing show an annual seroconversion rate of 1.5% (Koch and Adler, 1989).

. Currently there is no vaccine and there is no specific treatment for this disease. The initial symptoms can be treated using over counter medications, such as acetaminophen or ibuprofen. Those with weakened immune systems, such as AIDS patients may be given immunoglobulin intravenously (IVIG) to help the immune system. Infected People with severe anemia or aplastic crisis require hospitalization and blood transfusion (CDC) (Division of viral diseases).

. Since Structure based drug designing is now a popular technique used for increasing the speed of drug designing process. This was made possible by the availability of many protein structures which helped in developing tools to understand the structure function relationships, automated docking and virtual screening. Knowledge of structure based functional properties of a drug target is very essential for a successful *in silico* designing of drugs (Kishan K.V *et al.,* 2007).

Methodology

Retrieval of whole proteome of human *parvovirus B19* from NCBI

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Functional annotation of the proteome using SVMProt

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Prediction of antigenic peptides using Jemboss

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Proteomic analysis of the target protein using proteomic tools

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Modeling of target protein using MODELLER9V6

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Evaluation of modeled structure through PROCHECK and visualized through RASMOL

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Ligand selection and retrieval of the structures from PubChem

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Accelrys Discovery studio-Ligand fit was used for protein ligand docking

Results and Discussion

. The whole proteome of human *parvovirus b19* was retrieved from NCBI Refseq FTP server. The single-stranded genome contains 5596 nucleotides with the single nonstructural NS1 protein, two capsid proteins: VP1 and VP2. The RNAs expressed 7.5-Kda protein, 11-Kda protein and X protein. Structural protein VP1 shows that it is a coat protein belongs to calcium binding, zinc binding, magnesium binding and metal binding protein function families. Functions of 7.5kd protein and 11kd protein have not yet been determined experimentally. Analysis of 7.5kd protein by SVMProt shows that it belongs to outer membrane, lipid binding, coat protein, RNA binding structural protein (matrix protein, viral occlusion body, keratin) function families. It acts as an enzyme oxidoreductases-acting on a sulfur group of donars, isomerases –cis-trans isomerases.

. The VP1 protein of human *parvovirus b19* was identified as drug target because it is non homologous to the human, SVMProt gave function families and Jemboss antigenic server results gave highest antigenic sites. Three dimensional structure of VP1 protein was modeled using MODELLER9V6 (Figure 2) and the stereo quality of the predicted model was evaluated using PROCHECK in ADIT server (Figure 1). Twenty five binding sites are present in the VP1protein using Discovery studio Ligand fit. The ligand search was made through the literature search. Mitotic cyclins and cyclin b1 were chosen as potential ligand for drug candidate identification. Ligand Structures of different mitotic cyclins and cyclin b1 (teniposide, etopside, zinc03925951, zinc03978071, AFB epoxide and Aflatoxin) were selected for the study. These structures were retrieved from PubChem and used for the docking studies.

. The best docking complex formed with teniposide at the first binding site of the VP1 protein using Discovery studio 2.0 with best docking score 65.98 (Figure 3). Hydrogen bonds play an important role for the structure and function of biological molecules. Serine 580 was formed hydrogen bond with the ligand (Figure 4). Part of an epitope identified using Jemboss and the hydrophobic residues (PRO557, LEU555) and hydrophilic residue (Serine 554) of VP1 protein were involved in docking interaction. So it may be suggested for potential drug design.
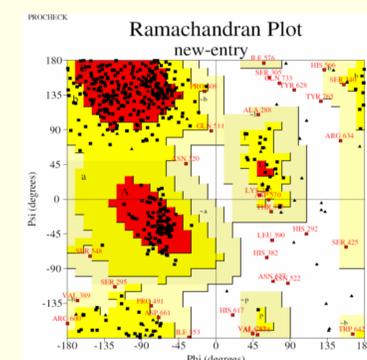

Figure 1: RAMACHANDRAN PLOT FOR VP1 PROTEIN OF HUMAN *PARVOVIRUS B19*

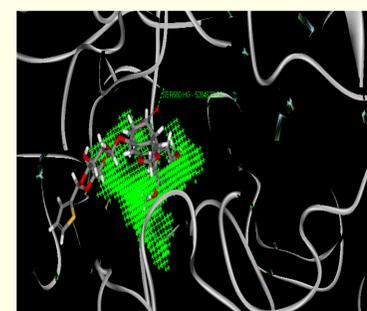Figure 2: RASMOL VIEW OF VP1 PROTEIN OF HUMAN *PARVOVIRUS B19* STRUCTURE

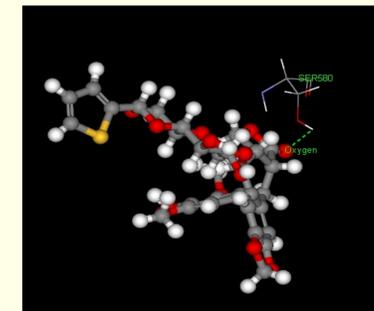Figure 3: LIGAND BINDING AT THE BINDING SITE OF THE VP1 PROTEIN

Figure 4: HYDROGEN BOND BETWEEN THE VP1 PROTEIN WITH LIGAND

Energy minimized value	-30206.28177kcal
Number of binding sites	25
Number of poses found	10
Best ligand docking pose	1
Docking run elapsed time	4.29
Docking score	65.98
Number of hydrogen bonds	1

CONCLUSION

The VP1 protein of human *parvovirus b19* is useful for the structural integrity in the virus. VP1 protein was selected as drug target due to the structural integrity presence of more antigenic peptides and human non homologous protein. The 3D structure of VP1 protein of human *parvovirus b19* was constructed through homology modeling by using MODELLER9V6 and validated using PROCHECK. The energy minimization was done for the modeled structure and used for further docking. The Docking studies were performed with six ligand molecules. The first pose of the docking complex of VP1 protein with the teniposide was giving the best docking score 65.98 and it may be suggested as a putative lead molecule based on the docking score. Hydrogen bonds play an important role for the structure and function of biological molecules. It was found that Ser580 was the residue forming hydrogen bond with the VP1 protein. The hydrophobic residues (PRO557, LEU555) and hydrophilic residue (Serine 554) of VP1 protein involved in docking interaction are also part of an epitope predicted using Jemboss. Thus, it strengthens the teniposide lead molecule as drug candidate against *parvovirus*. But, further studies are required such as ADMET studies to confirm the activity of the molecule which needs to be tested for biological activity before entering into human clinical trials.