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COMPUTATIONAL SYNTHETIC PEPTIDE VACCINE DESIGNING AGAINST GASTROENTERITIS DISEASE THROUGH REVERSE VACCINOLOGY APPROACH

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ABSTRACT: Aeromonas hydrophila subsp. Dhakensis a causative agent of gastroenteritis disease present in Diarrheal faeces. Computational research for peptide vaccine against aeromonal protein has been Published. In this study, the complete genome sequence of a virulent Aeromonas hydrophila strain was retrieved from genomic database. We screened the genome and identify the protein which was least similar to the human. Antigen determinant peptide was predicted with different databases and ASA calculation. Identified antigen was designed 3D model and simulation was performed in discovery studio from the docking study. We identify LATL determinant were the best peptide having CDocker energy 76.1367Kcal/mol. As this peptide was transmembrane protein it can be best potential vaccine.

KEYWORDS: Peptide vaccine, Epitope design, Gastroenteritis, Docking, minimization and Reverse vaccinology.

INTRODUCTION

Gastroenteritis is a diarrheal disease that occurs from bacteria as well as viruses. Bacteria like Aeromonas hydrophila subsp. Dhakensis infection Resulting in some combination of diarrhea, vomiting and abdominal pain and cramping. It is estimated that three to five billion cases of gastroenteritis occur globally on an annual basis, primarily affecting children and those in the developing world. It resulted in about 1.3 million deaths in children less than five as of 2008, with most of these occurring in the world's poorest nations.

Gastroenteritis has many causes, Viruses and bacteria are the most common. The infectious agents can come from outside your body or internally from some abnormal condition. For example, both normal and disease-causing intestinal bacteria may grow when antacids or other medication alter the stomach acidity. Viruses and bacteria are very contagious and can spread through contaminated food or water. In up to 50% of diarrheal outbreaks, no specific agent is found. Improper hand washing following a bowel movement or handling a diaper can spread the disease from person to person. Gastroenteritis caused by viruses may last 1-2 days. On the other hand, bacterial cases can last a week or more.

Reverse Vaccinology:

The process of vaccine discovery starts in Insilco using the genetic information rather than the pathogen itself, this novel process can be named as reverse vaccinology. The reverse approach to vaccine development takes advantage of the genome sequence of the pathogen. The genome sequence provides at once a catalog of virtually all protein antigens that the pathogen can express at any time. As this approach starts from the genomic sequence, by computer analysis, predicts those antigens that are most likely to be vaccine candidates.

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MATERIALS AND METHOD

To identify the Aeromonas pathogenic protein sequence for their antigenic properties the bioinformatics tools are used. The complete protein sequence of Aeromonas hydrophila subsp. Dhakensis was extracted from JCVI CMR (TIGRhttp://www.tigr.org) in the FASTA format. SDSC biological workbench is used for the purpose of screening the complete protein sequence. The least identity of the protein sequence was found by screening the protein sequence. The protein sequence which having least identity is used to find the epitope. The antigenic determinants (epitope) are found out by using EMBOSS antigenic. MAPPP (MHC-I Antigenic Peptide Processing Prediction) is used for binding prediction and proteasome cleavage prediction. This help to predict possible antigenic peptides to be processed and finally presented on the cell surfaces. The antigenic determinant having greater ASA (Accessible surface area) value is chosen to design a molecule by using discovery studio 2.5.

RESULT AND DISCUSSION

Screening:- The screening of protein sequence of Aeromonas hydrophila subsp. Dhakensis is done and the sequence having accession number AFH09486**.1** had least identity 25.484% is found. The sequence having least identity is chosen and used for finding antigenic determinants using Emboss Antigenic.

Identification of Epitope: The ASA values of the antigenic determinants were calculated. The antigenic determinant having greater ASA value is selected (Table 1). The result is compared with the MAPPP results for the binding of MHC 1 molecule (Table.3 & 4). The selected antigenic determinant is used to design the structure of epitope.

Minimization: The designing and minimization of MHC molecule is done by using Discovery studio 2.5. The epitope LATLKADVQLGVD is designed. The minimization energy of MHC molecule is found to be -28014.32249

Docking:- Docking is a method which predicts the preferred orientation of one molecule to a second when bound to each other to form a stable complex. Knowledge of the preferred orientation in turn may be used to predict the strength of association or binding affinity between two molecules. The epitope molecule is docked with MHC I molecule successfully is shown in the figure given below. The epitope molecule docked with MHC-I molecule successfully this shows that MHC I molecule represent the epitope to B cells. Cdocker energy of the interaction was found to be 76.1367Kcal/mol.

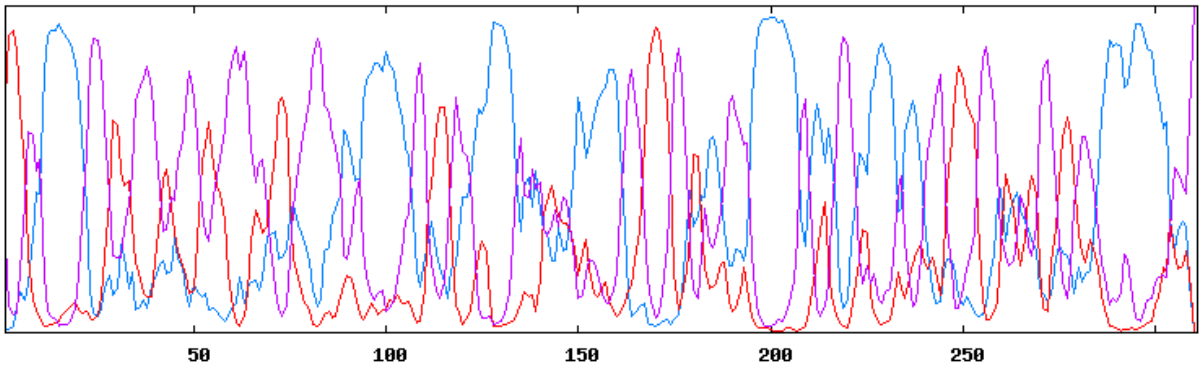
Emboss Result(Table .1)

#Sequence : AFH09486.1

Score 1.123 length 13 at residues 296->308

```
          *
Sequence: LATLKADVQLGVD
       |       |
 296       308
Max_score_pos: 307
ASA:30.76
```

Antigenic plot for sequence



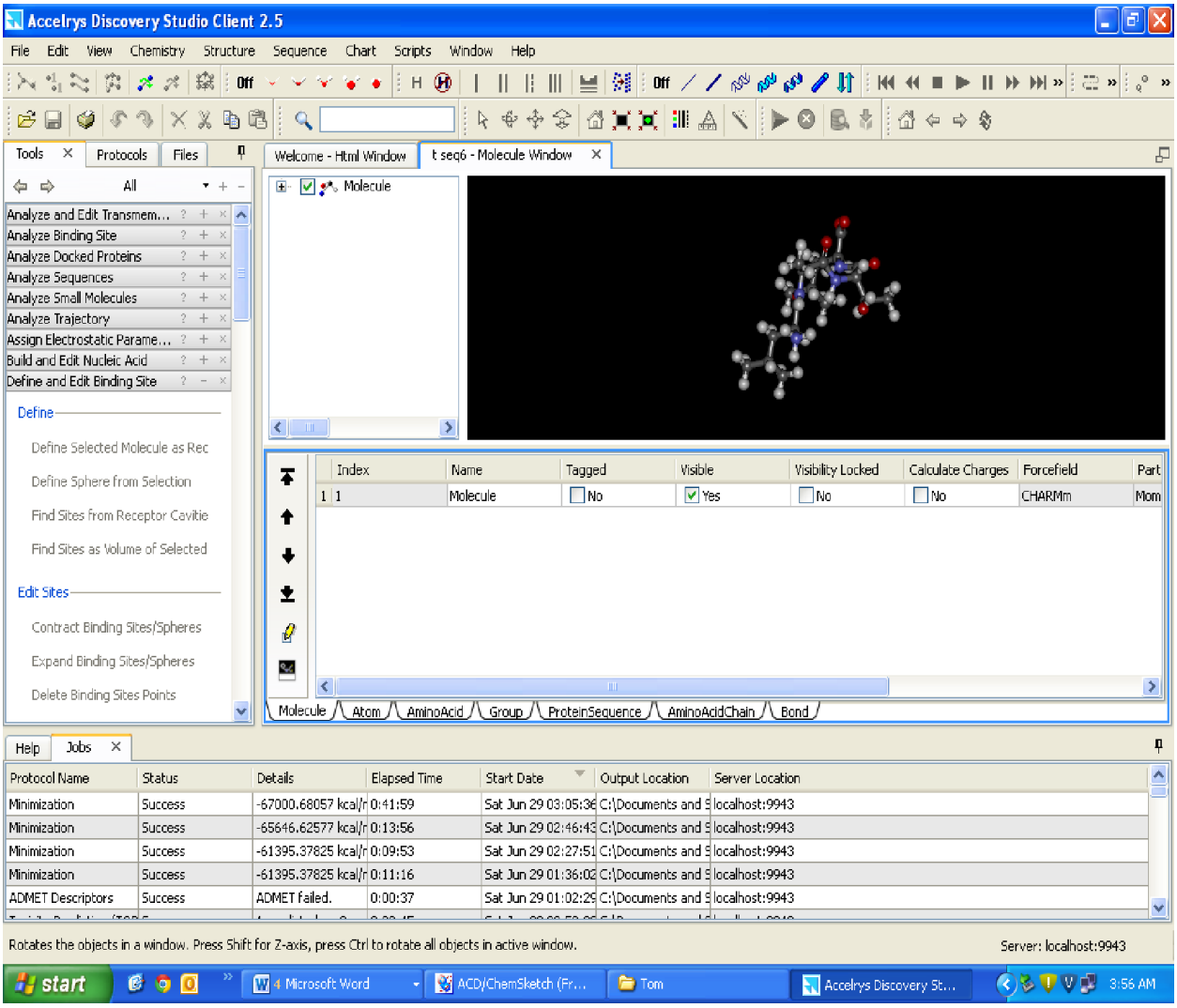
(Table.2) There are 13 antigenic determinants in your sequence:

N	Start Position	Sequence	End Position
1	12	IGQALALLLKN	22
2	26	AGSELSLYDIAPVTPGVAVDLSHIPTDVKVKG	57
3	63	PSPALVGADVVLISAGVAR	81
4	97	IVKNLVEKCAASCPKALIGIIT	118
5	121	VNTTVAIAAEVLKKAGV	137
6	142	RLFGVTTLDVIRAETFVAE	160
7	162	KGLNVDKVRVNVIGGHSGVTILPLLSQ	188
8	210	GTEVVEA	216
9	227	MGQAACRFGLSLIK	240
10	247	NVIECAYV	254
11	260	HATFFAQPILLG	271
12	274	GVETVLDYGKLSA	286
13	295	M**LATL**KADVQLGV	307

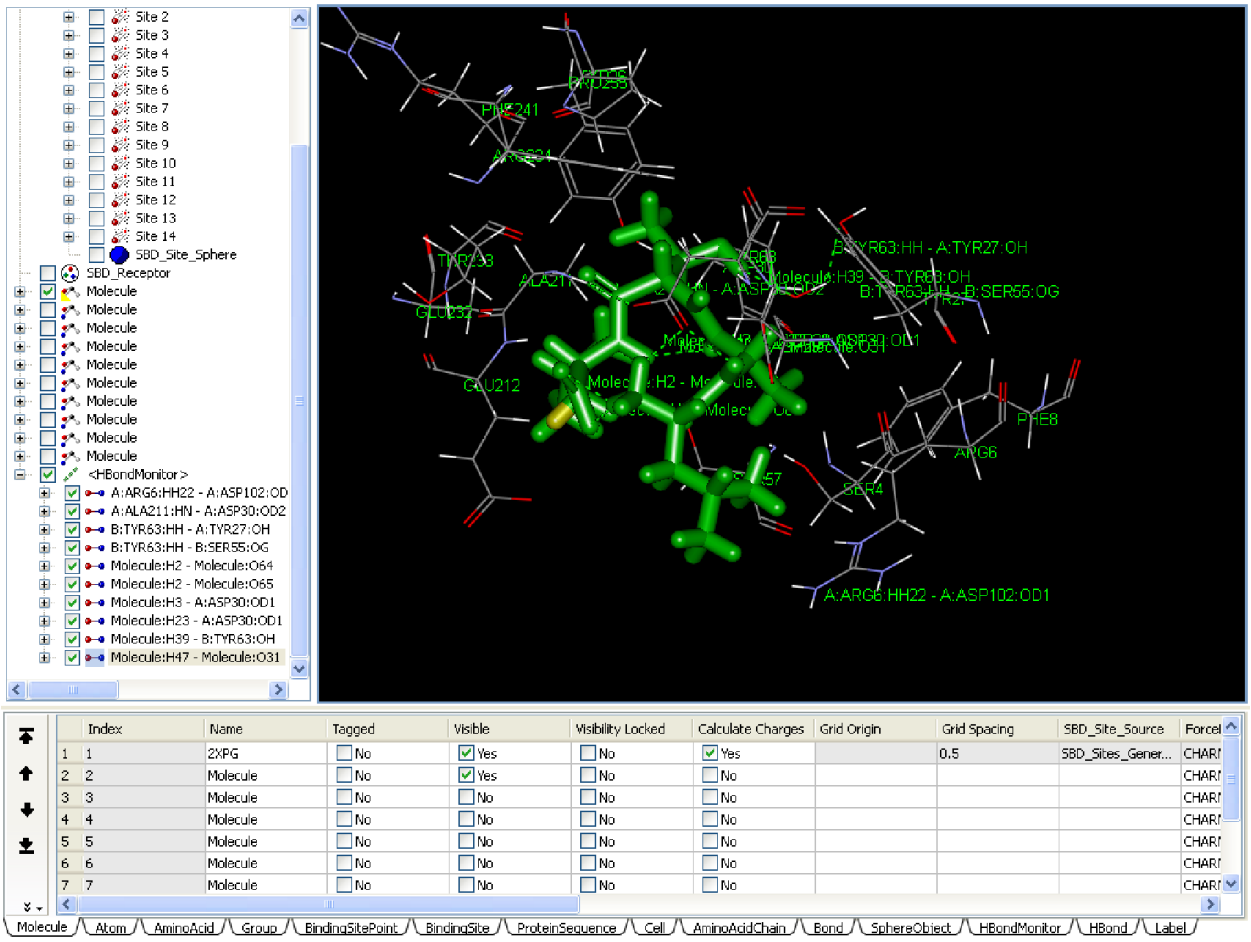
MAPPP

Query parameters	
Start with	Protein cleavage
Cleavage algorithm	FRAGPREDICT
Min. residue cleavage prob.	0.6
Min. fragment cleavage prob.	0.6
MHC binding matrices	SYFPEITHI
MHC type(s)	ALL
Min. binding score	0.6
Weight (cleavage:binding)	5:5

Query results							
Protein position	**Length**	**Sequence**					
Epitope	**Position**	**MHC type**	**n-mer**	**Overall score**	**Cleavage Probability**	**MHC binding score**	**Group**
0..310	311	MKVAVLGAAGGIGQALALLL..MDGMLATLKADIQLGVDFVK					
NRLPAGSEL	21	HLA_B_2705	9	0.8347	0.9937	0.6757	n-term. trimmed
NRLPAGSEL	21	HLA_B_2705	9	0.8378	1.0000	0.6757	n-term. trimmed
LPAGSELSL	23	HLA_B_0702	9	0.8571	1.0000	0.7143	same length
LPAGSELSL	23	H2_Ld	9	0.8871	1.0000	0.7742	same length
LPAGSELSL	23	HLA_B_0702	9	0.8388	0.9634	0.7143	c-term. trimmed
LPAGSELSL	23	H2_Ld	9	0.8688	0.9634	0.7742	c-term. trimmed
LPAGSELSL	23	HLA_B_0702	9	0.8571	1.0000	0.7143	c-term. trimmed
LPAGSELSL	23	HLA_B_0702	9	0.8571	1.0000	0.7143	c-term. trimmed
LPAGSELSL	23	H2_Ld	9	0.8871	1.0000	0.7742	c-term. trimmed
SELSLYDI	27	H2_Kk	8	0.8833	1.0000	0.7667	trimmed twice
APVTPGVAV	35	HLA_B_0702	9	0.8566	0.9988	0.7143	n-term. trimmed
NINAGIVKNL	91	HLA_A_0201	10	0.8234	0.9997	0.6471	n-term. trimmed
GIITNPVNTT	114	HLA_A_0201	10	0.8235	1.0000	0.6471	n-term. trimmed
EVLKKAGVY	129	HLA_A3	9	0.8256	1.0000	0.6512	trimmed twice
EVLKKAGVY	129	HLA_A3	9	0.8256	1.0000	0.6512	c-term. trimmed
RRLFGVTTL	140	HLA_B_2705	9	0.9324	1.0000	0.8649	n-term. trimmed
RRLFGVTTL	140	HLA_B_2705	9	0.9324	1.0000	0.8649	trimmed twice
AEAKGLNV	158	H2_Kk	8	0.8667	1.0000	0.7333	n-term. trimmed
TILPLLSQI	180	HLA_A_0201	9	0.8470	0.9995	0.6944	c-term. trimmed
TVLDYGKL	276	H2_Kb	8	0.8534	0.9971	0.7097	c-term. trimmed
AMDGM**LATL**	290	HLA_A_0201	9	0.9167	1.0000	0.8333	n-term. trimmed



(Fig.1)Minimization of Antigenic Epitope



(Fig.2)Docking result

CONCLUSION

Gastroenteritis is a diarrheal disease that occurs from Aeromonas hydrophila subsp.Dhakensis infection Resulting in some combination of diarrhea, vomiting and abdominal pain and cramping. It is estimated that three to five billion cases of gastroenteritis occur globally on an annual basis, primarily affecting children and those in the developing world. It resulted in about 1.3 million deaths in children less than five as of 2008, with most of these occurring in the world's poorest nations.

We have found the complete proteome sequence of the pathogen using TIGR and screening was carried out by SDSC Biology Workbench. We got 25.484% Identity. Antigenic Determinant was predicted, from which we have designed the epitope which binds to the MHC 1 molecule and selected the docked sequence using Discovery studio.

Therefore, from the whole analysis concluded that this vaccine is the potent and also good for the further clinical studies.

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