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BIOINFORMATIC ANALYSIS OF HOST – PATHOGEN INTERACTION IN INFECTIOUS BURSAL DISEASE OF CHICKENS

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ABSTRACT: *The analysis of amino acid sequences of the Infectious Bursal Disease virus (IBDV) and chicken MHC II proteins was done to identify their features. Antigenicity plot of the 1011 residue long IBDV sequence revealed 38 potential antigenic sites of the virus. Eleven MHC II binding peptides of IBDV VP2 were also predicted. Protein interface recognition sites for IBDV VP2 and chicken MHC II were predicted using a software PIR. In case of IBDV VP2, 21 residues and in case of chicken MHC II, 26 residues were identified as very likely to be involved in protein interface formation. Protein docking of amino acid sequences of IBD Virus and chicken MHC II molecules indicated a possible receptor – ligand type relationship.*

KEYWORDS*:* Infectious Bursal Disease, IBD virus, bioinformatic analysis, MHC II, chicken, host -pathogen interaction.

INTRODUCTION

Infectious Bursal Disease (IBD) is an acute contagious viral disease affecting young chickens upto six weeks of age causing high morbidity but low mortality. IBD Virus (IBDV) selectively affects the B Lymphocytes of chickens. It destroys B cells in the bursa of Fabricius causing significant depression of the humoral immune response. However, the specific moiety on chicken B cells, which is the putative site of predilection for IBDV is not known yet. Bioinformatic studies were therefore undertaken to explore the basis of host – pathogen interaction in Infectious Bursal Disease of chickens. Such an analysis could yield important clues to the identity of molecular target of IBDV.

MATERIALS AND METHODS

Amino acid sequences of Infectious Bursal Disease virus and chicken MHC II proteins were analyzed using various programs. Potential antigenic epitopes and MHC II binding peptides of IBDV protein were predicted on the basis of hydrophilicity profile using ANTIGEN program. Protein interface recognition sites of the IBD virus and chicken MHC II proteins were analyzed using a public domain software PIR. PIER value indicates how likely a particular residue is to be involved into a protein interface formation, with higher values meaning higher probability. PIER value above 30 means very likely interface residues, and below 0 very unlikely interface residues. Buried residues were not included into prediction. Protein docking of IBDV VP2 and chicken MHC II molecules was done using ZDOCK program and visualization was done using PYMOL software. ZDOCK is a Fast Fourier Transform based protein docking program. It takes two PDB files and outputs the predicted structure of their complex. The top 2000 ranked predictions are returned. ZDOCK searches

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all possible binding modes in the translational and rotational space between the two proteins and evaluates each by an energy scoring function. Each protein's structure is converted to a digital signal and a Fast Fourier Transform technique reduces the computational time.

RESULTS AND DISCUSSION

The analysis of amino acid sequences of the Infectious Bursal Disease virus and chicken MHC II proteins was done to identify their features. Antigenicity plot of the 1011 residue long IBDV sequence revealed 38 potential antigenic sites of the virus (Table 1). The conserved heptapeptide of IBDV VP2 showed similarities to peptide amidase which interacts with chymotrypsin and to an uncharacterized antigen of *Leishmania major* and *Leishmania braziliensis* which infect macrophages. Eleven MHC II binding peptides of IBDV protein were identified (Table 2). Twenty one protein interface recognition sites of Infectious Bursal Disease viral proteins (Table 3) and 26 PIR sites of chicken MHC II (Table 4) were identified. Protein docking of amino acid sequences of IBD Virus and chicken MHC II molecules (Fig. 1 & 2) showed a good fit indicating a possible receptor – ligand type relationship.

The bioinformatic analyses yielded useful information on the identity, nature and functional aspects of putative molecular target of IBDV. Thirty eight potential antigenic sites and 11 MHC II binding peptides of IBDV protein were identified. Twenty six sites on chicken MHC II and 21 sites on IBDV proteins were identified as protein interface recognition sites. The protein docking studies suggest a possible receptor – ligand type of interaction between the IBDV VP2 and chicken MHC II protein. These studies offer valuable insight into the nature of the putative target and form the basis for useful and confirmatory experimental studies. Overall, the bioinformatic data lends credibility to the hypothesis that chicken MHC II molecule may be the possible target for IBDV binding on chicken lymphocytes and some other cells.

Table 1.: Predicted epitopes of IBDV VP2 protein

S/no.	Start position	Sequence	End position
1	8	TQQIVPFIRSLLM	20
2	54	SGLIVFFPGFPGSIVGAHYT	73
3	82	FDQMLLTAQNLPASYNYCRLVSRSLTVRS	110
4	113	LPGGVYAL	120
5	124	INAVTFQGSLSELTD	138
6	155	IGNVLVGEGVTVLSLPTSYDLGYVRLGDPIPAIG	188
7	190	DPKMVATC	197
8	201	DRPRVYTI	208
9	212	DDYQFSSQYQAGGVTITLFSAN	233
10	236	AITSLSIGGELVFQTSVQGLILGATIYLIG	265
11	267	DGTAVITRAVAA	278
12	291	PFNIVIPT	298
13	301	ITQPITSIKLEIVT	314
14	329	ASGSLAVTI	337
15	342	YPGALRPVTLVAYER	356
16	358	ATGSVVTVAGVSNF	371

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17	379	LAKNLVTE	386
18	425	YFMEVADLNSPLKIAG	440
19	446	DIIRALRRIAVPVVSTLFPPAAPLAH	471
20	473	IGEGVDYLLG	482
21	515	KGYEVVANLFQVPQNPVVDGILASPGILRG	544
22	546	HNLDCVLRE	554
23	556	ATLFPVVITT	565
24	578	KMFAVIE	584
25	604	SGHRVYGYAPDGVLPLET	621
26	623	RVYTVVPID	631
27	638	IMLSKDPIPPIVGS	651
28	653	GNLAIAYMDVFRPKVPIHVAM	673
29	692	KLATAHRLGLKLAG	705
30	733	RLPYLNLPYLP	743
31	748	RQYDLAM	754
32	764	ELESAVRA	771
33	774	AAANVDPLFQSALSVFM	790
34	866	GIYFATPEWVAL	877
35	904	YLDYVHAEK	912
36	917	SEGQILRAATSIYGA	931
37	936	EPPQAFIDEVAKVYEV	951
38	986	PKPNVPT	992

Table 2: Prediction of MHC II binding peptides of IBDV VP2

S. No.	MHC allele	IBDV sequence	Highest score achievable	Score	% of highest score
1	DRB1-0301	IGLDPKMVA	9.5	6.2000	65.26
2	DRB1-0306	IGLDPKMVA	8.8	5.9000	67.05
3	DRB1-0307	IGLDPKMVA	8.8	5.9000	67.05
4	DRB1-0308	IGLDPKMVA	8.8	5.9000	67.05
5	DRB1-0311	IGLDPKMVA	8.8	5.9000	67.05
6	DRB1-0806	VITRAVAAD	8.6	5.6000	65.12
7	DRB1-1107	IGLDPKMVA	9.1	6.2000	68.13
8	DRB1-1501	IVPFIRSLL	9.8	6.6000	67.35
9	DRB1-1501	IVFFPGFPG	9.8	6.4000	65.31
10	DRB1-1506	IVPFIRSLL	9.8	6.6000	67.35
11	DRB1-1506	IVFFPGFPG	9.8	6.4000	65.31

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Table 3: Protein Interface Recognition for Infectious Bursal Disease Virus VP2

Predicted Value	Residue
36.81727	I401
36.70108	L180
36.29184	V429
35.06256	S239
34.71988	L408
34.48246	D198
34.20683	Y425
33.10989	T196
32.7483	C197
32.19756	A195
32.11408	A430
32.01945	L120
32.01888	G181
31.85093	I67
31.84774	T238
31.73148	F422
31.52063	W414
30.74351	Y397
30.49986	A119
30.41444	E428
30.35846	I184

Table 4: Protein Interface Recognition for Chicken MHC II

Predicted Value	Residue
53.42156	C163
53.4101	G97
53.4084	I96
51.31669	L11
48.56099	I69
47.48835	I155
47.37849	I155
44.75022	F110
44.10455	L159
40.69265	H13
38.2912	M145
37.31268	L28
36.93901	G27
34.94236	A186
34.48542	L79

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34.44962	G26
34.32684	V188
34.17143	V187
33.73702	I65
32.61472	F14
32.57884	L12
32.26153	V274
31.88524	A141
31.46091	D75
31.13498	S94
31.0082	L151
30.07324	L158

Table 5. Prediction of protein - protein binding of the heptapeptide of IBDV VP2

Amino acid	**Score**
S	-28
W	-4
S	-34
A	-12
S	-29
G	-6
S	-20

Fig. Prediction of protein – protein binding of chicken MHC II protein

MAVLSGAAVPLLLLGVLGGVGAVLKPHVLLQAEFYQRSEG

P----------PP--PPPP-

PDKAWAQFGFHFDADELFHVELDAAQTVWRLPEFGRFASF

------P----------

EAQGALQNMAVGKQNLEVMIGNSNRSQQDFVTPELALFPA

-------P------P----------PP----------

EAVSLEEPNVLICYADKFWPPVATMEWRRNGAVVSEGVYD

---PPP---------P----------

SVYYGRPDLLFRKFSYLPFVPQRGDVYSCAVRHWGAEGPV

----P-P----PP----------

QRMWEPEVPEPPSESSATLWCAVGLAVGIAGIAAGTALIL

---------P----------

RAVRRNAANRQPGLL

---------PP--PP

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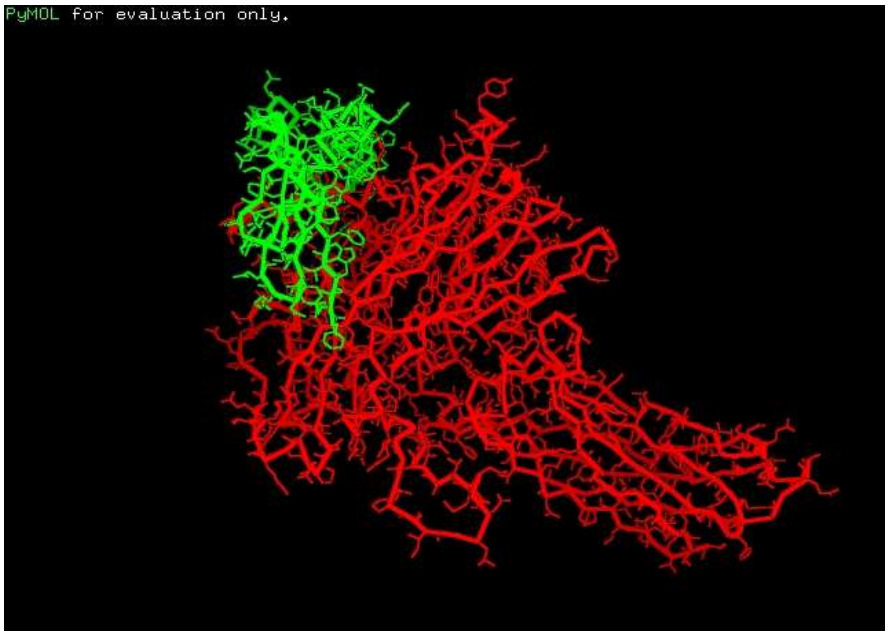

Fig. 1. A model of docking of IBD virus VP2 with chicken MHC II molecule.

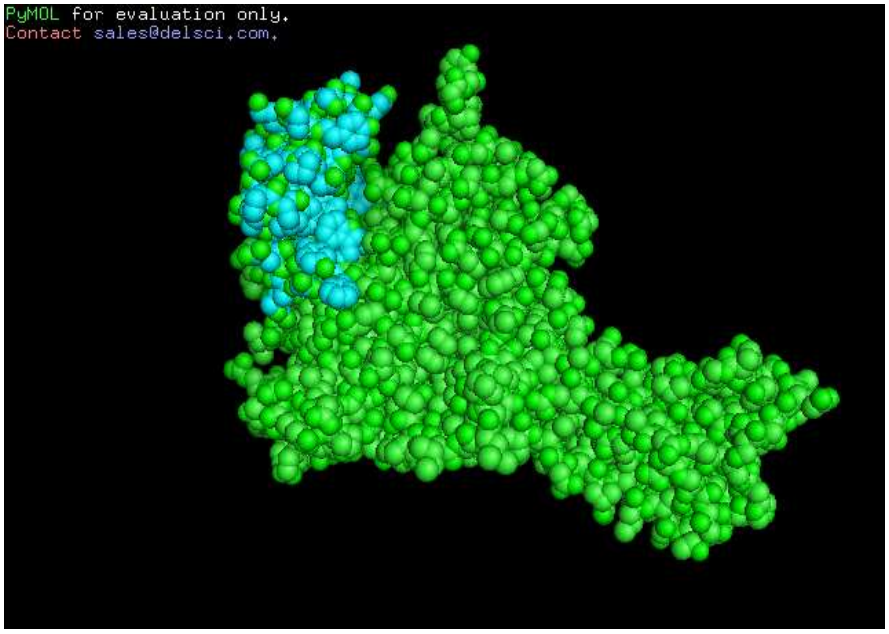

Fig. 2. Another view of a model of docking of IBDV VP2 with chicken MHC II molecule

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