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Review

Interactions of paramyxovirus: A review

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Abstract

Newcastle disease is one of the most common maladies that affect avian species and cause serious problems. The study was conducted to investigate the intracellular molecular interactions of paramyxovirus genome which take part in pathogenicity and create serious problems which affect poultry industry in particular chicken (broilers and layers). Also to know the main published ligands that attached to the receptors responsible for the Newcastle disease virus.

Keywords: Avian, Paramyxovirus

Introduction

Newcastle disease is highly contagious disease infected all of birds .And causes many infections in respiratory, intestine, neurological disease. Newcastle disease is diffuse worldwide and causes economic losses in poultry industry .It transmission by birds infection ,birds carriers ,infection birds organs and eggs (1). Incubation period is 3-4 days. Industry in Iraq have major economic loss because the endemic nature of the disease (2-6).

Etiology

Causative agent of ND is *Avian paramyxovirus which classified as follow:*

Classification

Phylum :Negarnaviricota
Class :Monjiviricetes
Order :Mononegavirales
Family :Paramyxoviridae
Sub family :paramyxovirinae
Genes :Aquaparamyxovirus , Avulavirus , Ferlavirus , Henipavirus , Mobillivirus , Respirovirus , Rubulavirus .

Avian paramyxovirus 1(APMV1) is single-stranded, negative-sense RNA virus in the family paramyxoviridae, non-segmented paramyxovirus particles are pleomorphic with lipid envelope and surround with spikes which is tightly cabbage to narrow filaments called the nucleocapsid .The nucleocapsid associated with matrix protein at layers lipid envelope. Made of 15,186 base. structural proteins are encode by specific genes in 3to 5 order, those structural prorteins are; nucleoprotein(NP), phosphoprotein (P), matrix (M), fusion (F), hemagglutinin neuramidase (7).

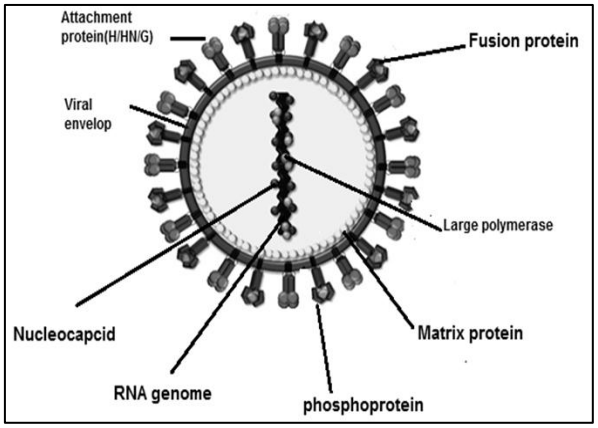

Figure (1):-Schematic view of paramyxovirus virion taken from Smith, Popa (8).

Explain structure of the virus.

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Three pathological types of Newcastle disease are available:-

Viscerotropic:-which infection of visceral of bird and causes green diarrhea.

Neurotropic:- which infection of nervous system and causes nervous signs e.g. torsion of neck and paralysis.

Neumotropic:- infection of respiratory system e.g. cough and nasal discharge (9-13). Symptoms of NDV in poultry depend on many factor, from these, the virus, host, species ,environmental, immune of birds and age of birds (14-18).

To sum, post mortem m lesion consist of hyperemia in intestine ,proventicular necrosis, edema and encephalomyelitis (19-23)

Proteins specific for Newcastle disease **pathogenicity**:

When enter of virus replication at point of enter of virus which causes viremia and lead to systemic infection (virulent strains). In (avirulentstrian) causes limited viral replication .Which pathogenesis depend on :-

Hemagglutinin–Neuramindase: this protein attached to sialic acid in host which have numerus function example major antigenic determinant of the virus .The protein capable to clump RBCs in vitro (24). paramyxovirus HN is require for F protein induced membrane fusion and membrane fusion is observed only when HN and F protein of the same virus or closely linked viruses are expressed in the same cell (25).

Fusion protein:

This protein attached to cell membrane in host . It long and encodes 553 amino acids long peptide precursors. Viral fusion protein was classified into two groups based on structure and mechanisms of fusion .The first category consists of pruning tools containing primor of F protein as well as the influenza hemagglutinin protein and retrovirus.F protein located near the cararboxyl terminus, and amino acid 25-30 typical cytoplasmic domain. Typical of paramyxovirus F proteins, the NDV F protein is a 553-amino -acid protein and is synthesized as a precursor, F0.The F0 must be proactively cleaved to F1 and F2 for fusion activity(26, 27). The tive precursor and proteolytic cleavage generates two subunits F1,F2 in case of paramyxovirus (28). The fusion (F) protein mediates immediately membrane to be fused. Perhaps the best proof of this conclusion is that some paramyxovirus F protein can guide this process by including the crystalline structure, indicating that the paramyxovirus fusion (F) and haemagglutinin-neuraminidase (HN) proteins of Newcastle disease virus (NDV) is multifunctional proteins that play critical roles during infection. The extend of NDV to replicate in macrophages and the contribution of the F and H Nproteins to NDV infection/ replication in are well addressed (29).

Pathogenicity of Newcastle disease:

Normally, the generation of new NDV are perfom under control and help of fusion protein F0, the latest one are cleaved into Fl and F2 in ordr to be pathogenic (30-32), proteases are mediate this post translation modification while trypsin capable of cleaving F0 for all NDV strains and in *vitro* treatment of non-infectious virus will turn it into ifective (33).

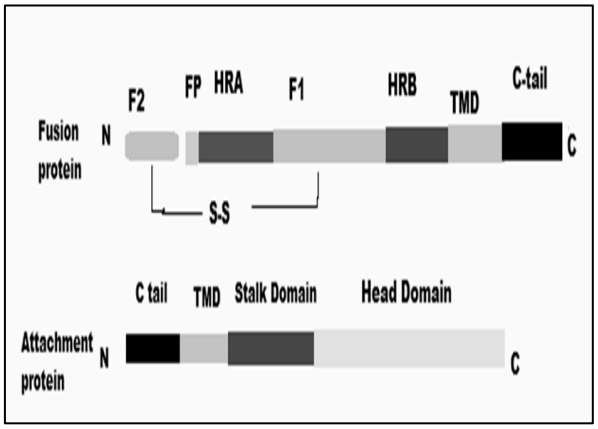

Figure (2) schematic view of Fusion and attachments proteins.

Adapted from (34)

(HR)heptadrepeatsequences,
(SS) signal sequence
(FP) fusion peptide
(TM)transmembrane domain
(CT) cytoplasmic tail or cytoplasmic domain

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Results:

From search using the word 'paramyxovirus' in RCSB PDBsearch engine we have got five structure (1usx,1usr,1e8t,1e8u,4G1O)and 8 ligand attached with them.From Search in RCSB PDB search engine we find the receptors specific for pathogeneses of Newcastle disease (Hemagglutinin –Neuramindase, Fusion protein). Search Parameter: Scop Tree search for Paramyxovirushemagglutinin-neurasminidase head domain. Hemagglutinin-Neuraminidase
Glycop Protein as represented by Chimera interactive molecular docking platform (35-37).

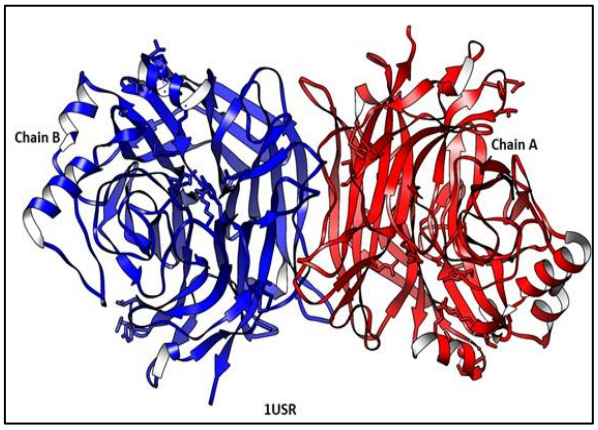


Figure (3): Second Sialic Acid Binding Site (38)

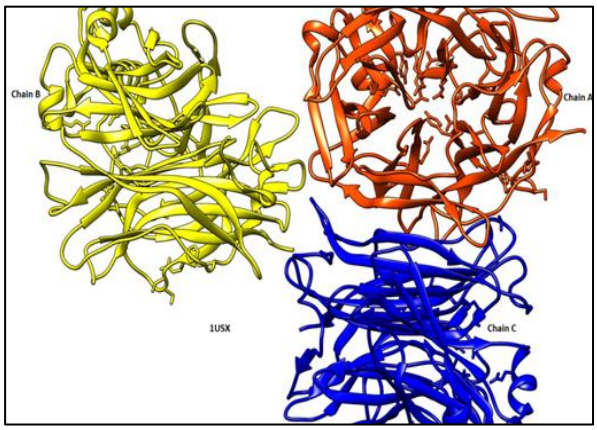


Figure (3):- Crystal structure of the Newcastle disease virus hemagglutinin-neuraminidase complexed with thiosialoside adapted from (38)

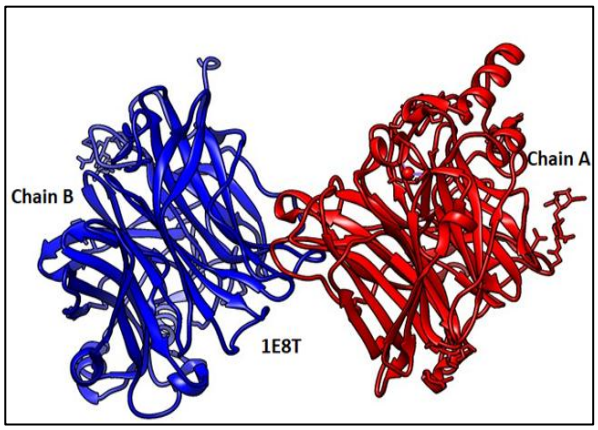


Figure (4):-Crystal structure of the multifunctional paramyxovirushemagglutinin-neuraminidase. (39)

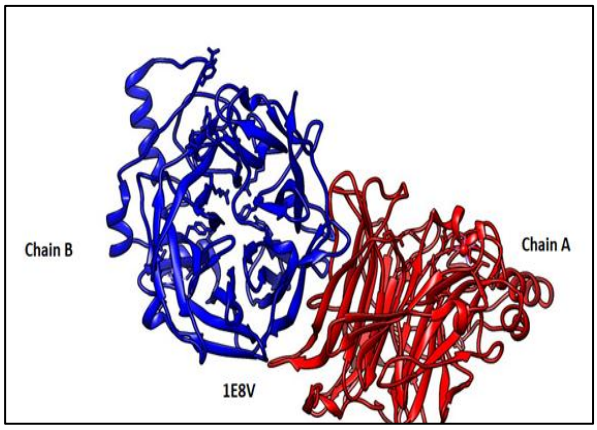
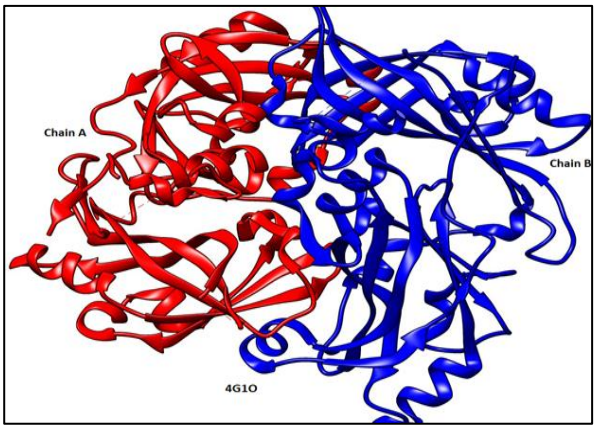


Figure (6):-Crystal structure of hemagglutinin-neuraminidase (39).



Figure(7):Crystal structure of Newcastle Disease virus matrix protein (40).

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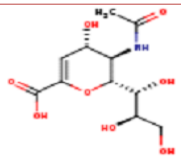
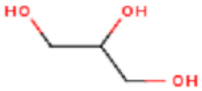
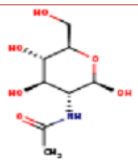
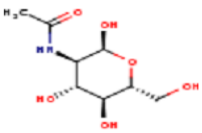
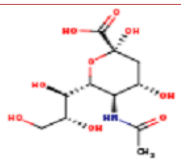
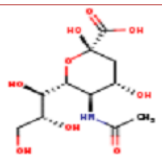
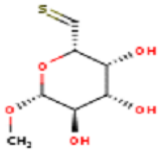
Regarding Search Parameters of Ligands associated with structures from: 'ScopTree Search for Paramyxovirushemagglutinin-neuraminidase head domain'Currently showing 1 - 8 of 8 .

Ligand Structure	ID / Formula / Name
Ca^{2+}	CA Ca CALCIUM ION
	DAN C11 H17 N O8 2-DEOXY-2,3-DEHYDRO-N-ACETYL-NEURAMINIC ACID
	GOL C3 H8 O3 GLYCEROL
	NAG C8 H15 N O6 N-ACETYL-D-GLUCOSAMINE
	NDG C8 H15 N O6 2-(ACETYLAMINO)-2-DEOXY-A-D-GLUCOPYRANOSE
	SIA C11 H19 N O9 O-SIALIC ACID
	SLB C11 H19 N O9 5-N-ACETYL-BETA-D-NEURAMINIC ACID
	**WIA** **C7 H12 O5 S** **METHYL(6S)-1-THIO-L-MANNO-HEXODIALDO-6,2-PYRANOSIDE**

Figure(8): types of ligands that attached with the receptor.

Taken from (PDB,2019)

Molecular studies

NDV V proteins suppress retinoic acid-inducible gene I (RIG-I)-like receptor (RLR)-which is responsible for controlling viruses through interferon pathway then enhance the virus pathogenicity (41). Some peptides have been designed to compete NDV ligand and in-vivo anhibit NDV pathogenicity and its growth (42). NDV F-proteins consists of heptad repeat domains HR1 and heptad repeat domains HR2, which responsible of

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its fusion activity. HR1 site of NDV fusion protein have "a" and "d" positions which modulate folding of the protein (43). NDV upregulates small basic C proteins (44). NDV lead to expression of the proopio-melanocortin gene (45). Also NDV inhibit (RLR) melanoma differentiation-associated protein 5 (MDA5) which modulate viral infection through natural immunity by interruption of signalosome structuring (46). He, Xing (47) have discovered the inhibitory effect of Beta-chitosan over NDV, while Shamaki, Sandabe (48) demonstrated that Ganoderma lucidum produces NDV inhibition by prevention NDV agglution of chicken RBCs via neuraminidase suppression.Experimentaly (49) have shown that NDV possess anticancer by modulating apoptosis (programmed cell death of cancer cells), through Expression of pro-apoptotic gene TRAIL and suppression of anti-apoptotic genes BCL2, BIRC3 and PRKCE.

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