A STUDY ON THE ANTIANTIGENICITY OF THE GLYCOPROTEINS ON THE MUMPS VIRUS AND HOW IT IS RELATED TO THE ACUTE AND INFECTIONS OF THE ENCEPHALITIS IN NEWBORN HAMSTERS

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ABSTRACT

The surface location of viral glycoproteins, their involvement in interactions with the cell and their role, reveal that these proteins are the antigens to which immunity develops if viral diseases are presented by immunological means. The F and the HN glycoproteins have their own specific activities. The discussion will concentrate mainly on the Kilham strains. The properties of the viral NANase influence the process of virus - induced cell fusion, and thus may contribute to cytopathology in tissue culture which correlates with the pathogenicity in vivo.

INTRODUCTION

All enveloped animal viruses have glycoproteins on the surface of the viral particle (virion). These viruses possess a membrane consisting of a lipid bilayer with glycoproteins projecting from the external surface. A nonglycosylated protein associated with the inner surface of the bilayer might be present - this is only true in some not all viral membranes.

Both the proteins and lipid of the viral membrane originate from the different sources : the proteins are virus-specified whereas the lipid of the viral membrane is derived from the host cell membrane during the assembly of the virus by a budding process. The number of glycoproteins present on the viral membrane varies from one species to another for example the membrane of paramyxoviruses are associated with two glycoproteins.

The surface of the virion of the paramyxoviruses have spike-like projections which is the glyoproteins. The

glycoproteins, like any other enveloped viruses, are anchored in the viral membrane by the interaction of a hydrophobic portion of the protein located at the base of the spike, with the lipid of the membrane. Studies show that the glycoprotein molecules possess enzymatic activities. Upon assembling on the membrane of the host cells, the synthesized glycoproteins form the viral envelope. The number of structural polypeptides present is six, the two glycoproteins are the major nucleocapsid-associated protein (NP), two less prominent nucleocapsid-associated proteins (P and L), and the membrane-associated or matrix (M) protein. The nonglycosylated proteins are internally located in the virion. They are found within infected cells and might explain why these nonglycosylated proteins are unlikely to be important targets of a protective immune response.

STRUCTURE OF GLYCOPROTEINS

The viral glycoproteins contain carbohydrate and the content ranges between 5% and 40%. It is now believed that similarity exists between the oligosaccharide moieties in the viral glycoproteins and in the glycoproteins of the host cell. Due to the size of the viral genomes being too small, in most cases, to specify glycosyl transverses and the glycosylation of the viral glycoproteins involves the glycosylating mechanisms of the host cell.

Studies show the presence of two different types of oligosaccharide moieties in the viral glycoproteins. The first, "high-mannose" type, contains N-acetyl-glucosamine and mannose, whereas the second, "complex" type contains galactose, fucose and sialic acid. Both types of glycoprotein possess a core unit composed of mannose and N-acetylglucosamine that is followed by branches. The difference in the branches between the two types is the branches of the complex type contain additional residues of N-acetylglucosamine, galactose and sialic asid. Normally, sialic acid is situated at the end of the oligosaccharide side chain. In both types the oligosaccharide is attached to the polypeptide chain by a β-N-glycosidic linkage between asparagine and N-acetyl-glucosamine. Some glycoprotein molecules possess neuraminidase activity but these molecule lack sialic acid (HN glycoprotein).

Non-ionic detergent such as Triton can extract the spike glycoproteins easily since they are integral membrane proteins. Proteolytic enzymes may destroy intact virion thus digesting

the spike glycoproteins. Spikeless virion possess peptide with a molecular weight of 5,000 - 9,000. The peptide originates from the spike glycoprotein and the fingerprint analysis proves it. Amino acid analysis shows that the peptide is rich in hydrophobic amino acids. This peptide is a portion of the lipid bilayer spike glycoprotein is impenetrable by the proteases, an indication that the peptide is buried inside the viral envlope. This shields can interact with a lipid bilayer since it has a hydrophobic nature. A hydrophobic peptide segment associates the viral glycoproteins with the lipid bilayer of the envelope.

The large hdyrophobic peptide fragment spans the lipid bilayer - showing that the viral glycoprotein is a transmembrane proteins. The enveloped viruses possess spike glycoprotein which are actually transmembrane proteins with carboxy termini spanning the lipid bilayer. Some parts of the carboxy terminus is sensitive to proteolytic digestion due to the exposure of terminus to the cytoplasmic side of the membrane. The distribution of the viral glycoproteins on the cell surface has been studied by electron microscopic analysis of cell surfaces containing antiviral antibodies conjugated with hemoccyanin or ferritin. Patches observed on the cell surface are actually aggregation of the glycoprotein molecules. The F and the HN glycoproteins have their own specific subtopic. Under each subtopic, a summary on how F and HN can affect the host cells in relation to the infectivity will be discussed.

The mumps virus has six strains : Enders, RW, O'Tate, Kilham, MJ and Jerryl Lynn B. strains. This paper will only concentrate on the Kilham strains. The MJ and RW strains are two non-adapted, low passage isolates. The Kilham strain is a neuro - adapted strain whereas the Enders and Jerryl strains are the two chick - adapted strains.

THE HN GLYCOPROTEIN

The larger glycoprotein of mumps virus is designated HN (Hemagglutinin-Neuraminidase). It is present on the surface of the virion of a dimer glycopeptides with a molecular weight of 64,000; the disulfide bonds held together the polypeptide chains in the hydrophilic region and hydrophobic bonds held together the chains at their bases (Figure 1).

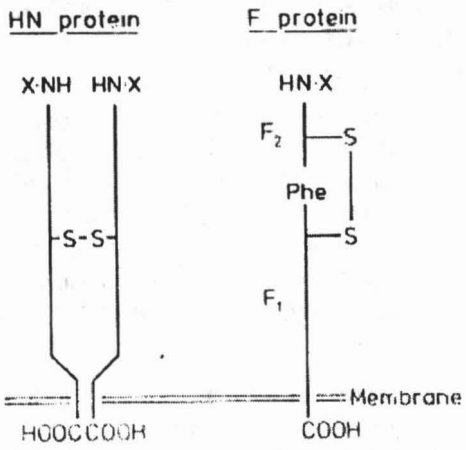

Figure 1

The HN protein has been shown to possess receptor-binding activity (usually referred to as hemagglutinating activity because of the use of the erythrocyte as a model cell) and enzymatic (neuraminidase) activity. There is a possibility that the same active site is involved in both receptor binding and neuraminidase

The largest viral glycoprotein, as suggested by Orvel (1978), mediates the activities such as hemagglutination, neuraminidase and adsorption. The glycoprotein is indeed required for infectivity. This seems to be a general rule for paramyxoviruses since it agrees with the finding with 3 different paramyxoviruses, SV5, NDV, and Sendai (Choppin, Scheid 1980). Both neuraminidase activity and the hemagglutination activity are properties of a single glycoprotein.

ADSORPTION

In order for the virus to start an infection, adsorption is a prerequisite. A specific receptor is required by the virus and it determines cell, tissue and organ tropism of the virus. The HN possesses a binding function mediating virus adsorption to the cell surface. It also possesses an enzyme activity, which

by eliminating natural neuraminic acid (NANA) - containing receptors on infected cell glycoconjugates , allows for efficient dissemination of progeny virions.

Virus is able to adsorp host cells, erythrocytes and soluble molecules. Regardless of the adsorption site, a receptor containing neuraminic acid residues is involved. Receptors such as glycoproteins from cell membranes and various soluble glycoproteins from serum, salivary glands, urine and glycolipids (gangliosides) incorporated into liposomes contain neuraminic acid. Therefore neuraminic acid is an important component of a receptor.

Other properties of adsorption is it is temperature independent, requires cations and occurs over a broad range of pH. Most of the paramyxoviruses elute rapidly from receptor at 37°C. This is an indication that the location of the receptor-binding function, which is capable of cleaving neuraminic acid from the receptor and thus destroying it. The number of neuraminic acid residues required for adsorption varies among virus strains but interestingly, all paramyxoviruses, most importantly, the mumps virus adsorb to neuraminic acid - containing receptors.

The availability of specific receptors on cells C and therefore virus adsorption might not be an important determinant of host that neuraminic acid-containing glycoproteins and glycolipids and ubiquitous on the surface of vertebrate cells.

BIOCHEMICAL FEATURES OF MUMPS VIRUS NEURAMINIDASES AND THEIR RELATIONSHIP WITH PATHOGENICITY

In the replicative cyle of the mumps virus, viral neuraminidase plays a role. In order for the virus to adsorp or penetrate, no enzyme is required, this is also the case during the assembly of the virus particle or its release from the infected cells. The viral neuraminidase plays a role in promoting the efficient spread of the virus by allowing virions to become dissociated from neuraminic acid - containing glycoproteins, whether they be constituents of the cell surface, soluble glycoproteins in mucous secretions or components of other virus particles.

Neuraminic acid residues normally are absent in the glycoproteins of mumps virus due to the presence of viral neuraminidase. Viral neuraminidase plays a role in preventing

the aggregation of progeny virus by removing potential virus receptors from their own glycoproteins.

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The virus hemagglutination activities (HA) and the elution rates for adsorbed virions are consistent with the NANase properties. All mumps virus strains show different responses towards agglutination of the erythocytes when treated with NaCl. The Kilham strains, in particular, are not affected by the NaCl concentration in agglutinating the erythrocytes and adsorbed Kilham strains virus elute less rapidly from erythrocytes. There appears to be a correlation between these properties, associated with the HN glycoproteins, with the cytopathogenicity of the strains. This is confirmed in the studies, done by Mc Carthy and Johnson (1980), Wolinsky et. al (1985) and Mc Carthy et al (1980) on several strains of mumps with respect to their constituent structural polypeptides, cytopathology and neurovirulence.

It is noted that there are no significant differences in the structural proteins of strains. It is also noted in these strains of mumps virus, in particular the absence of inactive F glycoprotein (F_o) in progeny virions. Thus the strains of mumps virus can be divided into separate categories, those with efficient, active NANases. Each strains has its own NANase kinetics for enzymes. The Kilham strain has a less efficient and less active NANase, meaning that the strains with less active, NANases have longer half - lives of adsorption. This shows that various strains will elute from cells via NANase activity at different rates. The fastest to be eluted are those strains with active NANase and the less active NANase will be eluted the slowest.

Upon incubation at 37°C, a certain amount of virus-mediated hemolysis occurs. This is an indication that virus-erythrocyte fusion is taking place. This process might affect the observed elution kinetics due to the incorporation of some adsorbed virus into the erythrocyte membrane upon fusion Consequently the virus-erythrocyte fusion becomes refractory to NANase, the Kilham strains are more readily cause cell fusion in culture The release of adsorbed virus for these strains are delayed and this might affect a loss of elutable virus upon fusion with the erythrocytes (Merz and Wolinsky 1981)). This strains nave the capability of causing extensive cell fusion in tissue disseminate to brain after

peripheral inoculation (Wolinsky and Stroop, 1988). It is also neurovirulent, meaning that the involvement of the neurons after gaining entrance to the central nervous system (CNS)

Studies by Merz and Wolinsky (1981) suggest that Kilham strains mumps virus NANase activity contributes to cytopathology, thus they come to the conclusion that nonfusing strains possess an active NANase and elute rapidly from erythrocytes, whereas the fusing strains of mumps virus have a less active NANase and slower elution rates from erythrocytes. Evidently, the result suggest that the properties of the viral NANase influence the process of virus-induced cell fusion and thus may contribute to cytopathology in tissue culture which correlates with the pathogenicity in vivo.

The kinetic properties of NANases and the consequent elution properties of the different mumps virus strains paralled the observed in vitro cytopathology. The strains with an active NANase cause little cytopathology and no cell fusion in CV -1 cells, in contrast, infection with those strains having less active NANase cause intensive cell fusion. Consequently, the HN glycoprotein activity determining, in part, the cytopathology as a consequence of a relatively prolonged association of progeny virions with the plasma membranes of adjacent infected and uninfected cells resulting in an increased cell fusion potential. Conversely, strains with an active NANase will be associated with the cell surface for a shorter tissue internal resulting in a reduced potential to induce cell fusion An active NANase promotes rapid release of progeny virions, so that no cell fusion occurs and the action of a less active NANase prolonging the association of progeny virus with the infected cell surface, increasing the likelihood of cell fusion. According to Choppin and Scheid (1980) the activity is proven to be partly true. Viral NANase can contribute to the full expression of the F proteins activity. This is consistent with what is previously observed by Bratt and Gallagher (1972) using NDV.

The NDV NANase contributes to virus - induced cell fusion. Neurath and coworkers (1972) demonstrate that the inhibition of Sendai virus NANases activity increases hemolytic activity. This is a clear indication that fusion is more pronounced in the absence of the NANase activity of the HN glycoprotein. The NANase activity is detrimental to virus-mediated cell fusion.

F GLYCOPROTEIN

The exact sequence of events in the penetration of enveloped viruses into cells is still not clear in many instances. Fusion of viral and cell membranes and phagocytosis (viropexis) having been suggested as mechanisms of penetration. In the case of paramyxoviruses, it is now clear that fusion of viral and cell membranes is involved in the penetration step and that penetration is mediated by a viral glycoprotein.

The virus is able to undergo multiple - cycle replication and to spread in a host and therefore in order to cause disease is dependent upon repeated rounds of successfull adsorption and penetration, the role in the pathogenesis of virus infection is played by the viral glycoproteins. The penetration step does appear to be an important determinant of the tropism of paramyxovirus.

The F protein is involved in the activities known to be associated with the viral envelope, i.e. the cell fusion and hemolysis. Experiments in defective systems carried out by Choppin and Compans (1975) and that of Homma in Japan (1973), give an initial proof that the F protein is indeed involved in these activities.

The active F glycoprotein, which consists of 2 disulfide - linked polypeptides, F_1 and F_2, arises from an inactive precursor F_o by protease activation. The biologically important result of this cleavage is that it activates viral infectivity and virus - induced cell fusion and hemolysis. Therefore, the activation of these biological activities of the virus is dependent on the cleavage of a viral surface glycoprotein by a host enzyme. The fusing activity enables the initiation of an infection by fusion of the viral envlope with cellular membranes and enhances the development of an infection by promoting cell - to - cell spread via synctium formation. The cytopathic effects and virulence attributable to a paramyxovirus have been shown to be in part related to F glycoprotein activity.

Studies show that persistence of the inactive F_o forms, whether due to the inability of the host cells to cleave F_o to an insensitivity of the F_o precursor to proteolytic activation results in a limited, non cytopathic infection. Such an infection can be transformed to a cytopathic infection capable of further propagation, by the addition of a protease capable of cleaving F_o to the active F glycoprotein. Results from the experiments carried out by Sheid and Choppin

(1977), Merz et al (1981). Nagai et al (1981), Klenk et al (1978), Örvel (1981) show that the mumps F_o precursor is completely cleaved in infected cells, resulting in its absence in purified infection virions of both non - fusing ang fusing strains

The fact that activation of the infectivity of the virus parallels that activation of cell membrane fusion and hemolysis which involves fusion of the viral and erythrocyte membranes provides evidence regarding both the mechanism of the activation of infectivity and the step in virus replication that is involved in this activation.

Adsorption of virions containing the uncleaved F_o protein to receptors on the cell membrane occurs normally because adsorption of infectivity is at a step beyond adsorption, but before the transcription of the viral RNA. The step is virus penetration and the fact that infectivity is activated by the same process as membrane fusion provides strong evidence for the previous hypothesis that the mechanism of penetration of mumps virus is fusion of the viral membranes.

The ability of a particular virus strain to cause cell fusion during the course of an infection must result from some mechanism(s) in addition to proteolytic cleavage of the F glycoprotein. Choppin (1964) reported that proteolytic cleavage of virus products with the same range of activities. By analog the lack of the internally mediated cell fusion from the non - fusing mumps strains could represent differential sensitivity of the F_o glycoprotein to host cell proteases. Alternatively, the activity of HN glycoprotein modify the expression of the active F glycoprotein function since the tissue culture cell fusion activity of mumps virus has been shown to correlate with virus - associated neuraminidase activity (as discussed under neuraminidase activity)

The paramyxovirus mediate the fusion of lipid bilayers through the action of the F glycoprotein. This fusion activity is manifested in 2 general ways :

I. externally mediated fusion which can result in hemolysis 'fusion from without', and virus penetration of the cell and

II. internally mediated post infection cell fusion and synctia formation (fusion from within)

Conformational differences between the F_o and F glycoproteins are likely to be present since the monoclonal Ab specific for the F glycoprotein did not recognize the F_o form which was recognized by the monospecific anti - f_{ab}.

The role of cleavage of the glycoprotein in the biological activities of the virus is summarized in Fig 2.

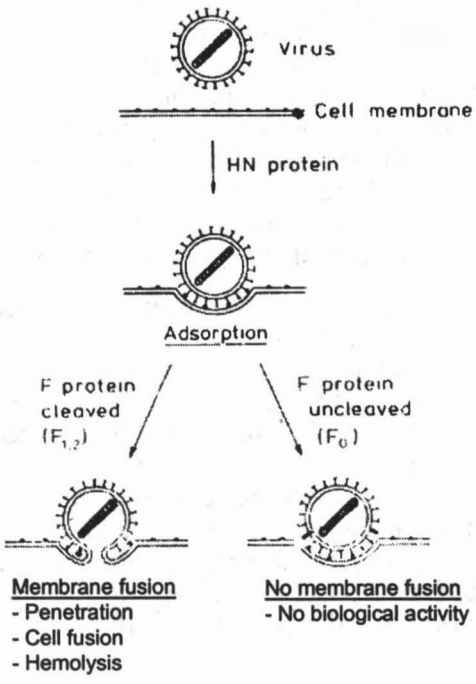

Figure 2.

The roles of the paramyxovirus glycoproteins in the initiation of infection.

The HN protein mediates the adsorption of the virus to the receptors on the cell membrane. The virus are able to penetrate into the cell by means of fusion of viral and cell membranes mediated by the F protein. First the F protein is cleaved into two subunits, F_1 and F_2 in order to be active. Penetration is not possible unless the F protein is cleaved. The virus will only adsorb. Cleavage of the F protein not only makes penetration possible but also activates the ability of the virus to cause cell fusion and hemolysis.

The finding that the activation of hemolysis and cell - fusing activities occur together on cleavage of tne 2 activities is a result of similar biochemical mechanisms. The cleavage of the precursor molecule requires specific host -

derived proteases. The structure of the glycoprotein determines the susceptibility of the precursor molecule to these proteases.

From the protease activation mutants of a paramyxovirus findings, the conclusions that host - dependent cleavage of F_o is required for activation of infectivity, cell fusion and hemolysis and that host range and tissue tropism are found to be true (from studies with the mutants and wild - type Sendai virus). For example, although the F_o proteins are Sendai Virus cannot be cleaved by a protease in MDBK (NDV) are cleaves in these cells. Plasma membrane has been associated as the location of the enzyme - has not been established conclusively. Also, findings show that cleavage may not always occur at the plasma membrance.

When the F_o protein of virus that is adsorbed to the cells is not cleaved, the cells are not infected unless protease is added to the medium. This is the case when the activating protease is present and capable of cleaving the F_o during replication but does not have access to adsorbed virus. The cells in one tissue, is an infected host, were capable of activating inactive viration produced by other cells, failure of cleavage of the F_o proteins by virus - producing cells would be activated during adsorption to other cells. If the cells have the appropriate protease, this would certainly limit the spread of infection . This fact is important.

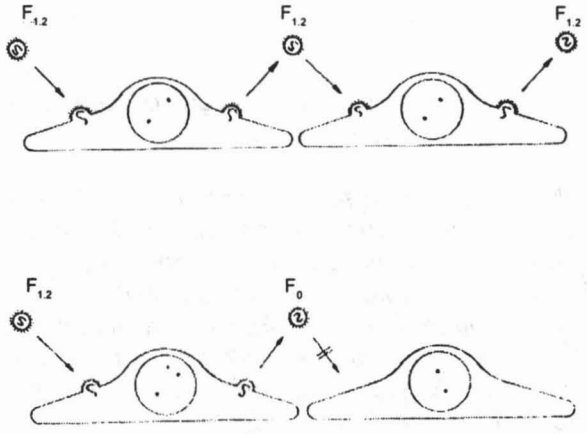

Figure 3. Cleavage of the F protein in causing the spread of infection.

Top : The infectious virus particle with cleaved F protein ($F_{1,2}$) infecting a cell possessing a protease capable of cleaving

the F protein of progeny virus particles, producing another infectious virus and thus spreading to other cells.

Bottom : When a cell without an appropriate activating protease is infected, the progeny virus possess an uncleaved protein (F_o) and result in being noninfectious. Therefore the spread of infection results in a dead-end situation.

From Figure 3 we can see that the host range and the ability of the virus to initiate infection and to undergo multiple - cycle replication and spread in the host are dependent on proteolytic and spread in the host are dependent on proteolytic cleavage by a host enzyme. This is proven definitely within the findings with the cell culture are chick embryo systems. This also indicates, that the viral virulence in the adult animal is dependent on proteolytic activation of the virus (extensive studies by Nagai).

In addition to their roles in adsorption and penetration, the glycoproteins of some viruses has been shown to be important determinants of host range and virulence, and in the case of the mumps virus, this has been related to specific proteolytic cleavage of a viral glycoprotein that activates the ability of the virus to initiate infection and consequently to undergo multiple - cycle replication and spread in the host. This is the outcome of an encounter between the virus and the host dependent on the proper match between the susceptibility of the viral glycoprotein to cleavage by a protease and the availability of that protease in the host cleavage of the precursors of the spike proteins of the virus occurs extracellularly. Although formation of viral particles is not dependent on the cleavage of the precursors molecule for these viruses, a number of biological activities of these glycoproteins, i.e. cell fusion, hemolysis, hemagglutination neuraminidase activity and virion infectivity are dependent on the occurence of proteolytic cleavage, thus viral particles containing uncleaved precursor glycoprotein do not exhibit any of these biological properties.

THE KILHAM STRAIN MUMPS VIRUS REPLICATION IN THE CENTRAL NERVOUS SYSTEM (ACUTE PHASE) OF MUMPS VIRUS ENCEPHALITIS IN SUCKLING HAMSTERS

Newborn hamsters were inoculated intraperitoneally with the neuroadapter mumps virus (Wolinsky et al (1976)). After 6th day of illness, petechiae were seen scattered over the cortices of many animals. After coronal sectioning, similar hemorrhages were sometimes seen in deep gray structures.

Hydrocephalus could be observed as early as the 9th day of the illness. This early mild to moderate hydrocephalus occured independently of any demonstrable aqueducted sternosis. There is a perivascular inflammatory infiltrates with or without associated small hemorrhages especially prominent in gray matter. Mild meningeal inflammation, diffuse ependymitis (most prominent in the aqueduct and third ventricle) and mild choroiditis were noted. Limited neuronal necrosis with attendant parencymal inflammatory change was present, scattered throughout the neuraxis. This change was especially prominent in hippocampa regions. Viral nucleocapsids were first visualised on the 2nd day of the infection. They tended to occur in small aggregates. As the days passed (after the innoculation) the aggregates be coming more frequent and larger.The inclusions became enlarged as the infection proceeded.

There was a marked tendency for the nucleocapsids to become associated with the plasma membrane of infected cells. Viral nucleocapsids aligned beneath the cytoplasmic membrane of infected cells. At such sites of viral alignment, morphologic were observed in the cytoplasmic. Trilaminar membrane (of the cytoplasmic membrane) was thickened to 45 to 55 Å , and the entire membrane measured 90 to 100 Å. Small spike - like processes were noted on the outer surface of the plasma membrane. The virus - cytoplasmic membrane complexes appeared to be the earliest change to occur at sites of viral budding.

Distinctive lamellae of smooth endoplasmic reticulum were observed by the 4th of infection these structures were usually intimately associated with nucleocapsids and the presence of such lamellae in the cytoplasm of a cell appeared to reflect the presence of mumps virus material. With further development of the infection the lamellae become organized into concentric whorls. The rnajor native components of the infected cells remained undisturbed until relatively late in the acute phase of the infection. Early disruption and desquamation of ependymal and choroidal cells were seen by the 6th day Marked vacuolation of cytoplasmic organelles of neurons was evident as early as the 8th day and probably marked impending cell death.

Macrophages were often encountered on choroidal and ependymal surfaces after 11th day of the infection. They often contained multiple and sometimes contained typical mumps virus virions. The virus effectively spreads into the neural parenchyma whereas in comparison to result obtained from an experiment with the non - neuroadapted virus it

remains relatively confined to ependymal cells. Also, there is no alignment of the nucleocapsids has ever been observed in natural form from non - neuroadapter mumps virus - infected animals. These virus - cytoplasmic membrane complexes are the apparent precursor sites of virion formation by the process of budding. This difference may be a major factor in enabling the neuroadapted virus strains to spread from the choroid and ependyma to invade neuron and other cellular elements of the brain.

Virions formation from the ventricular surfaces of ependymal and choroidal cells, as observed in the neuroadapted mumps virus (e.g. Kilham strain) infection would seem to provide an efficient means viral dissemination via the bathing cerobrospinal fluid to sites throughout the CNS.

Evagination of the virus - cell membrane complex to form filamentous virions at both free apposing distant and continuous spread of mumps virus in the nervous system. In addition, the finding of virus along dendrites at a considerable distance from the perikarya of neurons suggest intraneural transfer of the virus.

These varied observation would suggest that the membrane induction by mumps, although not a specific marker of the virus, if a reflection of altered cellular metabolism.

Once gaining entry into macrophages, the viral nucleocapsids shows altered morphology.

ULTRASTRUCTURE OF THE CHRONIC INFECTION

Conversion from an acute productive phase of infection to a chronic, non productive phase of infection in this model has ultrastructural correlates that appear to justify persistent paramyxoviral infections of brain (Wolinsky, (1997)).

Occasionally, plasma cells could be found below the ependyma of the lateral ventricles throughout the interval of observation, providing evidence of persistent inflammatory response and possibly on going antibody formation within the central nervous system. Viral nucleocapsids were not found within these cells (posterior third ventricle).

Cytoplasmic aggregates of typical paramyxovirus nucleocapsids, identical in appearance and location with those seen during the acute phase of infection, were found

in ependymal cells of the third ventricle and aqueduct for long as 33 days postinoculation. Late persistence of viral nucleocapsid in neurons was not seen. Virus - related alterations of the cytoplasmic membranes and viral maturation by budding from the surface of infected cells was not demonstrated.

This pattern of an acute phase of infection during which maturation of virus can be readily shown followed by a chronic phase in which only cytoplasmic aggregates of nucleocapsid are seen appears to be characteristic of paramyxoviral infections that establish persistence in brain.

Many members of the paramyxovirus group show a propensity for replication in ependymal cells. In several of these animal model systems, hydrocephalus secondary to the aqueductal stenosis has been a prominent sequelae of the ependymal infection. Receptors for the mumps virus must be present at the sites on the outer surface of the ependymal cell plasmalemma in order to enable viral adsorption and penetration. The distribution is unknown. Current suggestion indicates that the sites for the receptors of mumps virus involve the plasmalemma of ependymal cell cilia. This could allow the cilia of ependymal cells of closely related apposed venticular surfaces to be cross-linked by viral particle bridges and possibly initiate cell fusion across ventricular surfaces at these sites. Fusion is favoured by a high concentration of viral particles. This is actually what is occuring in the aqueduct. It is continually being bathed by the cerebrospinal fluid where many of the maturing virions are released. The resultant deformation of the ventricular system could then lead to impaired circulation of cerebrospinal fluid and progressive hydrocephalus.

The hemagglutinin-neuraminidase (HN) anf fusion (F) glycproteins molecules project from the surfaces of mumps virions and mumps virus-infected cells. The HN and F glycoproteins are likely candidate targets of protective humoral and cellular immune responses. It has been found that these viral glycoproteins are involved in the early interactions between the virions and the cells. The interactions are; adsorption to the cell surface and penetration of the involvement of the glycoproteins in causing cytopathic effects, involvements in interactions with the cell, and has a role as determinant of tropism. The ability of virus to spread and these interactions of glycoproteins has shown to be important determinants or pathogenicity of the virus. The involvement of the glycoproteins in these activities is not unexpected because of their location on the surface of the virion.

Due to the location of viral glycoproteins, their involvement in interactions with the cell, and their role, it would be expected that these proteins would represent the antigens to which immunity must be developed if viral diseases are to be prevented by immunological means. This has indeed been shown to be the case wherever it has been investigated.

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