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REVIEW ARTICLE

Cellular receptors for viruses: links to tropism and pathogenesis

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Introduction

The interaction of a virus with its cellular receptor initiates a chain of dynamic events that will enable entry of the virus into the cell. In addition to the fact that the virus–receptor interaction is a multistep process in itself, multiple attachment receptors may be used sequentially, or in a cell-type-specific manner, and co-receptors may also be involved (for a review, see Haywood, 1994). It is beyond the scope of this article to give a complete review of cellular receptors for viruses. The data presented have, therefore, been selected to focus attention on those virus–receptor interactions that provide links to virus tropism and pathogenesis.

For most viruses, the receptor distribution in an individual is wider than the observed tissue tropism. Also, many virus–receptor interactions determine the host range and therefore constitute an interspecies barrier. Although mutations can accumulate rapidly, especially in RNA viruses, tolerable changes in the viral envelope proteins are constrained by the need to interact with a certain receptor. However, eventually, such changes may drastically alter the tropism and virulence of a virus. Furthermore, even in non-infected cells, the virus–receptor interaction may induce signal transduction, resulting in cytokine secretion, apoptosis, stimulation of the immune response, or, conversely, immunosuppression.

Virus tropism and pathogenicity are multifactorial

The term ‘entry’ for the first step of a virus life-cycle describes the various ways a virus can get into a cell and can be taken to mean pH-independent fusion at the cell surface, pH-dependent fusion in acidic endosomes, uptake of non-enveloped virions by endocytosis or the conformational changes leading to the uncoating of the viral genome (Fig. 1). The general concept of a ‘spring-loaded’ metastable state and conformational changes induced by low pH or binding of a virus to its receptor has been developed using influenza virus haemagglutinin (HA) and seems to be valid for a variety of viruses (for reviews, see Skehel *et al.*, 1994; Steinhauer *et al.*, 1992; White *et al.*, 1994). Thus, HA switches from a native non-fusogenic to a fusogenic conformation, which is induced by exposure to acidic pH in the endosome. This conformational change can also be achieved by exposing HA to heat or denaturing agents such as urea, suggesting that the native structure of the molecule is trapped in a metastable state and that the fusogenic conformation is released by destabilization of the native structure. Coupling the energetically expensive process of membrane fusion to an energetically favourable conformational change drives the reaction (Carr *et al.*, 1997). Similar fusion (F)-protein structures have been found in the influenza virus HA, simian parainfluenza virus 5 F, human immunodeficiency virus (HIV) gp41, mouse moloney leukaemia virus envelope transmembrane protein, and Ebola virus gp2 protein (Baker *et al.*, 1999 and references therein). Although structurally different, the tick-borne encephalitis virus (TBEV) E protein is also functionally analogous (Rey *et al.*, 1995; Stiasny *et al.*, 1996).

Although the virus–receptor interaction is needed to initiate infection, pathogenesis is a multistep process and the development of disease is influenced by the intracellular milieu, induced cell functions such as the capacity of the host to develop a proper immune response, the velocity of virus replication, cytopathogenicity and the spread of infection within and between organs, which again may or may not depend on the presence of specific cellular receptors. Even when infection does not proceed, virus–receptor-mediated signal transduction may induce the secretion of cytokines, such as interferons, which can have a great impact on the development of a disease. For example, enveloped viruses such as HIV and herpes simplex virus (HSV) can induce interferon-α via the mannose receptor on dendritic cells or monocytes (Milone & Fitzgerald-Bocarsly, 1998). This interaction induces signals in cells important for the immune system, but it does not lead to the uptake of viruses.

The budding and the release of viruses can also have a decisive impact on pathogenesis by determining the parameters of virus spread. This is obvious for pantropic viruses such as influenza or Sendai. The uptake and release of these viruses in polarized epithelial cells of the respiratory tract is restricted to the apical side. This is an important factor in preventing systemic infection. In contrast, viruses that are released basolaterally may spread systemically (for a review, see Compans, 1995).

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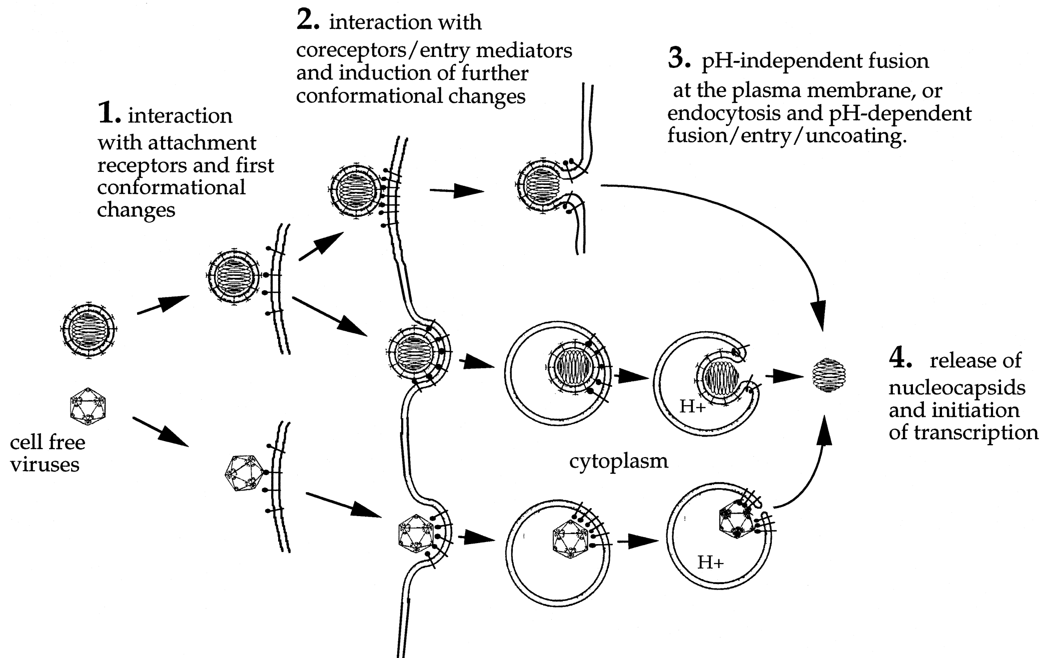

Fig. 1. Four steps of virus entry into target cells. The interaction of the virion with the attachment receptor leads to the first conformational changes in the viral envelope proteins (1). This step enables the interaction with co-receptors, or entry mediators, and further conformational changes at the plasma membrane (2), which may deliver the energy for membrane fusion (3). Several viruses require the low pH in acidic endosomes to induce this conformational change. These mechanisms lead to the release and possibly the uncoating of the virus genome, and the initiation of the virus replication cycle (4).

The primary infection usually involves a small initial dose of virus and leads to little impact for the host. Replication of virus within the initial site of infection will then lead to a substantial multiplication of virus particles and considerable damage in secondary target organs. For the spread of virus to different organs and cell types, the use of multiple receptors might be advantageous. Viruses may either have the intrinsic capacity to use more than one receptor, as found for complex viruses such as herpes viruses (Tufaro, 1997), or they may change their capacity to bind to receptors or co-receptors by mutation of their envelope proteins. Both mechanisms are observed during HIV infection.

Receptor usage and the pathogenesis of HIV

CD4 has been found to act as the primary receptor for HIV (Klatzmann *et al*., 1984). In recent years, rapid progress has been made in identifying a set of chemokine receptors, which belong to a family of G-protein-coupled seven-transmembrane proteins, that represent co-receptors for HIV infection. Although not all factors are known yet, it appears that macrophage-tropic, T-cell-tropic and dual-tropic HIV strains use certain sets of co-receptors: macrophage-tropic strains primarily use CCR5, and T-cell-tropic strains primarily use CXCR4. In an infected individual, the co-receptor-determined tropism of the virus may change from macrophages or dendritic cells in mucosal tissues to a tropism for T cells. This change is due to mutations emerging in the viral envelope genes during progression of the infection (for a review, see Berger *et al*., 1999).

The concept of consecutive conformational changes is valid for HIV entry. The most favoured current model proposes that the initial binding of gp120 to CD4 induces a conformational change in gp120 which enables it to interact with a co-receptor. This interaction is supposed to induce a further conformational change in the viral envelope which results in the activation of gp41 and the positioning of its fusion active peptide in close proximity to the membrane and finally in the insertion of the fusion peptide into the membrane of the target cell. The dramatic conformational changes of gp120 have been confirmed by X-ray crystallographic studies (for a review, see Berger *et al*., 1999). As with influenza virus HA, the native HIV envelope protein gp120/gp41 complex appears to be trapped in a metastable state until the receptor interaction induces the transition to an energetically more favourable state. This conclusion is also supported by the enhancement of the infection with low concentrations of soluble CD4 or neutralizing antibodies which can facilitate structural alterations (Allan *et al*., 1990; Sullivan *et al*., 1995), and the inhibition of infection or cell–cell fusion by short peptides interacting with transiently exposed structures of the envelope proteins (Eckert *et al*., 1999 and references therein).

A major contribution to HIV pathogenesis (Fauci, 1993,

1996) is the presence of the attachment receptor, CD4, on cells central to the immune response, and its downregulation following infection (Aiken *et al*., 1994; Jabbar *et al*., 1990; Raja *et al*., 1994). Target cells for HIV are T helper cells, dendritic cells, including Langerhans' cells in the skin and in mucous membranes, and cells of the monocyte-macrophage lineage, including microglial cells in the brain. Dendritic cells present in the genital mucosa are now thought to be the first target cell in the host. They can transport the virus to lymph nodes and distribute it to contacting T cells possibly by circumventing co-receptor-dependent mechanisms (Hladik *et al*., 1999). Moreover, dendritic cells lose their immunostimulatory functions upon infection, which is the first step to immunodeficiency (for a review, see Knight & Patterson, 1997).

Glycoprotein 120 expressed on the surface of macrophages may induce apoptosis in lymphocytes via co-receptor interactions, which eventually contributes to the destruction of these immune cells (Herbein *et al*., 1998). In the CNS, receptors such as galactocerebroside (GalC; Bhat *et al*., 1991, 1993; Harouse *et al*., 1991) or co-receptors alone can interact with soluble gp120 and influence pathogenesis. Glycoprotein 41 has also been found to induce a proliferative inhibition in lymphocytes (for reviews, see Denner, 1998; Haraguchi *et al*., 1995). Synthetic peptides containing 17 amino acids of the gp41 sequence inhibit the mitogen-stimulated and the IL-2-dependent proliferation of T cells, the mixed lymphocyte reaction, and the respiratory burst and chemotaxis of monocytes. Attempts to identify cellular receptors mediating the suppressive effects are in progress but the mechanism has not yet been elucidated.

Interestingly, a natural co-receptor mutation exists which directly influences the interaction with HIV and which is of pathogenetic relevance. A 32 bp deletion in CCR5, which abolishes the virus site of interaction, may confer partial resistance to infection with macrophage-tropic HIV-1 to individuals who carry the mutation (Huang *et al*., 1996*b*; Liu *et al*., 1996; Samson *et al*., 1996). Haplotype analyses indicate that the mutated allele originated quite recently, approximately 700 years ago in northeastern Europe. The timing and distribution of the mutation suggest that a former epidemic, which exerted enormous selective pressure against CCR5, might have facilitated the rapid distribution of the 32 bp deletion (Libert *et al*., 1998; Stephens *et al*., 1998). It has been suggested that in addition to the reduced levels of CCR5, high levels of the chemokines MIP-1α, MIP-1β and RANTES may contribute to the clinical resistance or the slow progression of the disease in certain individuals. These findings may be exploited therapeutically by designing substances which block the co-receptor interaction with HIV, or by removing co-receptors by somatic gene therapy (Berger *et al*., 1999). Viruses expressing the cellular receptors CD4 and CXCR4 as envelope proteins have also been engineered to eliminate gp120-positive infected cells (Mebatsion *et al*., 1997; Schnell *et al*., 1997). Viruses bearing these molecules interact with HIV-1-infected cells in tissue culture and reduce HIV titres in infected T cell lines by a factor of 10000. However, the clinical application of such viruses appears questionable.

Competition for the same receptors: coxsackie viruses and adenoviruses

The non-enveloped capsids of picornaviruses can interact with a variety of cellular proteins (Table 1; Bergelson *et al*., 1994; Kuhn, 1997; Shafren, 1998; Triantafilou *et al*., 1999; Ward *et al*., 1994). Following binding, picornaviruses usually undergo several conformational changes leading to virus entry and uncoating of the genome (Arita *et al*., 1998; Dove & Racaniello, 1997; Kaplan *et al*., 1990; Racaniello, 1996). The geometry of the picornavirus and adenovirus interaction with the target cell surface is quite different. Depressions on the icosahedral capsids of some picornaviruses, the so-called canyons, were found to interact with cellular receptors, whereas attachment of adenoviruses is mediated by fibres with globular knobs at their tips projecting from the virus capsids. In spite of these structural differences, some viruses of both families compete for the same receptor, CAR (coxsackie virus–adenovirus receptor; Bergelson *et al*., 1997; Roelvink *et al*., 1998). CAR is a 46 kDa transmembrane protein belonging to the immunoglobulin superfamily and containing two extracellular domains. When transfected into hamster cells, this molecule mediates both attachment and entry of coxsackie virus B3 and B4 and adenoviruses 2 and 5 (Bergelson *et al*., 1997). The binding sites on the adenoviral fibre knobs for CAR have been identified recently, and might now be modelled to develop adenovirus vectors with altered tropism for gene therapy or as antiviral drugs (Bewley *et al*., 1999; Roelvink *et al*., 1999).

The attachment and uptake of serogroup C adenoviruses depends on two separate but co-operative events: the interaction of the fibre with an attachment receptor (CAR), and the interaction of the penton base with an internalization receptor, $\alpha_v\beta_3$ and $\alpha_v\beta_5$ integrins (Bergelson *et al*., 1997; Roelvink *et al*., 1998; Wickham *et al*., 1993). The penton base of adenovirus 2 may also interact with β_2-integrins as attachment receptors on the surface of haematopoietic cells (Huang *et al*., 1996*a*). Thus, CAR or β_2-integrins promote attachment of adenoviruses to cells, and α_v-integrins mediate their internalization via endosomes. Interestingly, some of the coxsackie virus B strains which use CD55 (decay-accelerating factor, DAF) as attachment receptor also require co-receptors of the integin family for virus entry (Agrez *et al*., 1997; Shafren *et al*., 1995).

In order to investigate the internalization mechanism, the three-dimensional structure of soluble recombinant $\alpha_v\beta_5$ molecules bound to adenovirus has been determined. The results suggest a precise spatial arrangement of the five arginine, glycine, asparagine (RGD)-containing protrusions on the penton base promoting integrin clustering and signalling

Table 1. Viruses and cellular receptors discussed in this review

Virus family (-group) virus*	Receptors	Distribution of receptors	Tropism of the virus	Associated diseases
Adenoviridae *(subgroup A,C,D,E,F)*				
adenovirus	CAR (Ig superfamily) $\alpha_v\beta_3$- and $\alpha_v\beta_5$-integrins	widely widely	epithelial cells, lymphoid cells	respiratory infection, lymphoid tissues
adenovirus C2	$\alpha_M\beta_2$-integrin	monocytes		
Arenaviridae				
LCMV (mouse/human)	α-dystroglycan	widely	lymphoid tissue, brain, other tissues (mouse)	febrile disease, lymphocytic choriomeningitis, persistent infection (mouse)
LFV	α-dystroglycan	widely	lymphoid tissue reticuloendothelial system	Lassa fever
Coronaviridae *(serogroup 1)*				
HCV-229E	hAPN	widely	respiratory tract	common cold
TGEV (pig)	pAPN		enteric tract	respiratory, enteric
FIPV (cat)	fAPN		hepatocytes	respiratory, enteric, hepatitis, neurologic
CCV (dog)	cAPN			enteric infection
(serogroup 2)				
HCV-OC43	sialic acid	widely	respiratory tract	common cold
MHV (mouse)	Bgp (Ig superfamily)	widely	hepatocytes, brain	respiratory, enteric, hepatitis, neurologic
BCV (cow)	9-*O*-acetyl-neuraminic acid	widely		enteric infection
(serogroup 3)				
IBV (chicken)	?			respiratory, hepatitis
Filoviridae				
Marburg virus	asialoglycoprotein receptor	hepatocytes	neutrophils, mononuclear cells, endothelial cells, hepatocytes	haemorrhagic fever
Flaviviridae				
dengue virus	heparan sulfate HAR FcγR ?	widely ? monocytes/macrophages	monocytes/macrophages	febrile illness, haemorrhagic fever, or shock syndrome
HCV	glycosaminoglycan (CD81 ?)	widely	hepatocytes	hepatitis, hepatocellular carcinoma
Hepadnaviridae				
HBV	(HBV-binding factor)		hepatocytes, PBMC, other tissues	hepatitis, hepatocellular carcinoma
DHBV (duck)	carboxypeptidase D (gp180)	widely		
Herpesviridae				
HSV-1, HSV-2	mannose-6-phosphate R heparan sulfate HveA (TNFRSF14) HveB/C/D (PVR family)	macrophages, DC widely widely	epithelial cells, neurons	skin lesions, latent neuronal infection, encephalitis (rare)
EBV	CD21 (CCP family)	B cells	B cells	infectious mononucleosis, Burkitt's lymphoma,
	second unknown receptor	?	epithelial cells	epitheloid carcinoma
Orthomyxoviridae				
influenza A virus	sialic acid	widely	respiratory tract	influenza
Paramyxoviridae				
measles virus	CD46 (CCP family) second unknown receptor	widely ?	respiratory tract, mononuclear cells, endothelial and brain cells	acute measles, acute encephalitis, and SSPE (rare)
CDV (dog)	?		respiratory tract, lymphoid tissues, brain	distemper, encephalomyelitis
NDV (chicken)	sialic acid			
Sendai V (mouse)	sialic acid	widely	epithelial cells	respiratory, enteric
Picornaviridae				
coxsackie virus (CV) A9	$\alpha_v\beta_3$-integrin, β_2-microglobulin	widely	gastrointestinal tract, other tissues	enteric infections, febrile illness, meningitis
CV A13,18,21	ICAM-1 (CD54; Ig superfamily)	widely		
CV B1,3,5	DAF (CD55; CCP family), $\alpha_v\beta_6$-integrin	widely		
CV B	CAR (Ig superfamily)	widely		
echovirus 1,8	$\alpha_2\beta_1$-integrin	widely	gastrointestinal tract, other tissues	febrile illness, meningitis
echovirus 6,7,11,12,13, 20,21,29,33	DAF (CD55; CCP family)	widely		
HAV	HAVcr-1 (Ig superfamily, mucin-like)	widely	gastrointestinal tract, liver salivary gland, kidney, spleen, lymphocytes	hepatitis
rhinovirus	ICAM-1, -2 (Ig superfamily)	widely	respiratory tract	common cold
poliovirus	PVR (Ig superfamily)	widely	epithelial cells neurons	enteric infection, poliomyelitis (in 1-5% of infections)
Retroviridae				
HIV	CD4 (Ig superfamily) and chemokine receptors (TM7) GalC (glycolipid)	macrophages, T cells, dendritic cells, microglia brain cells	CD4-positive cells, (m/T-tropic strains), few brain cells	lymphadenopathy, AIDS, encephalopathy
FIV (cat)	CXCR4 (TM7 family)			feline AIDS

* Unless indicated in brackets, the viruses infect humans. For explanations of abbreviations see text of the review.

events required for virus internalization (Chiu *et al.*, 1999). The interaction of integrins with RGD-containing peptides can induce caspases and apoptosis (Ruoslahti & Reed, 1999 and references therein). It is not known whether viruses also induce such signals via interaction with integrins.

Adenoviruses have the ability to infect a wide range of tissues and have been identified as the cause of diseases such as respiratory infections, epidemic keratoconjunctivitis, pneumonia, cryptic enteric infection and gastroenteritis (Wadell, 1990). As suggested earlier, the different tropisms of the

adenoviruses probably result from differential receptor usage. Based on the recent findings, chimeric adenoviruses with exchanged fibres or fibre knobs have been constructed to target infections to certain tissues (Stevenson *et al*., 1997).

Poliovirus: species tropism, but not tissue tropism, is determined by receptors

All three serotypes of poliovirus replicate initially in cells of the oropharyngeal and enteric tract. In the minority of cases (1–5%), virus then invades the CNS, destroys motor neurons and induces myelitis and paralysis. What role do cellular receptors have in the pathogenesis of the disease? The human poliovirus receptor (hPVR, CD155) belongs to the Ig superfamily. It contains three Ig-like extracellular domains and is expressed in four splice variants designated hPVR-*α*, -*β*, -*γ*, -*δ* (Bernhardt *et al*., 1994; Koike *et al*., 1990; Mendelsohn *et al*., 1989). Domain 1 of hPVR is sufficient to bind the virus (for reviews, see Nomoto *et al*., 1994; Racaniello, 1996; Wimmer *et al*., 1994). The viral receptor-binding sites are amino acids located on the floor and at the rim of the canyon-like depressions in the capsid (Colston & Racaniello, 1994; Liao & Racaniello, 1997). It has been suggested that antibodies may not be able to recognize epitopes in this narrow cleft of the canyon and therefore the development of neutralizing antibodies is hampered (Chapman & Rosmann, 1993). Thus, the topography of the receptor-binding site may directly contribute to the pathogenicity.

In man, PVR proteins are expressed in many cells and tissues, including the small intestine, lung, liver, heart, neurons of the spinal cord and the motor end-plate of skeletal muscles (Freistadt, 1994; Leon-Monzon *et al*., 1995; Nomoto *et al*., 1994). Since liver, lung and heart are not normally considered to be replication sites of poliovirus, this observation indicates that the susceptibility of tissues to poliovirus is not determined merely by the distribution of PVR. The susceptibility of PVR-positive mononuclear cells in the blood may play a role in the eventual CNS invasion (Freistadt *et al*., 1993). However, it remains to be investigated which of the PVR isoforms are expressed by which cell type and how the expression is correlated with infection during poliomyelitis. A mouse homologue of hPVR does not bind poliovirus, including those viruses adapted to mice. Thus, hPVR determines the species tropism of poliovirus (for a review, see Nomoto *et al*., 1994).

In hPVR-transgenic mice, poliovirus induces neurological defects similar to those observed in man. This is a perfect animal model to test the neurovirulence of various poliovirus strains (Deatly *et al*., 1999; Koike *et al*., 1991; Ren *et al*., 1990). Neurons, and not glial cells, were found to be infected and paralysis is caused by direct destruction of motor neurons. Interestingly, in both man and transgenic mice, the neurotropism of poliovirus cannot be explained solely by the tissue distribution of the receptor. Molecular determinants of neurovirulence and attenuation have been located in the 5′-proximal 1122 nucleotides of the viral genome (Macadam *et al*., 1993). Most mutations in this part of the genome do not alter the receptor usage, but they influence the interaction with intracellular factors. The internal ribosomal entry site within the 5′ non-coding region significantly contributes to host range specificity and neurovirulence (Gromeier *et al*., 1999; Shiroki *et al*., 1997).

Members of the poliovirus receptor family are also used by α-herpesviruses as cell entry mediators

Cell entry by *α*-herpesviruses, which have a double-stranded DNA genome of approximately 152000 bp and encode more than 100 proteins is, in comparison to the smaller and simpler RNA viruses, a much more complex process. In most cases, five viral surface proteins (gB, gC, gD, gH and gL) interact with cellular receptors and mediate virus entry (for a review, see Spear, 1993). Several different cellular surface molecules have been identified as receptors which may act together, consecutively or independently, to effect the uptake of herpesviruses. These include heparan sulfate or chondroitin sulfate proteoglycans (Shieh *et al*., 1992; Shukla *et al*., 1999), mannose-6-phosphate receptors (Brunetti *et al*., 1995) and the herpesvirus entry mediators (Hve) A, B, C and D (Geraghty *et al*., 1998; Montgomery *et al*., 1996; Takahashi *et al*., 1999; Warner *et al*., 1998). HveA belongs to the tumour necrosis factor receptor family (TNFRSF14), whereas HveB, -C and -D belong to the PVR family. Heparan sulfate appears to be a necessary surface component for virus entry into primary neuronal cells (Immergluck *et al*., 1998). Is there a functional parallel between the receptor usage of poliovirus and *α*-herpesviruses resulting in the neurotropism of both viruses?

Heparan sulfate proteoglycans are used by several viruses as initial attachment receptors

The capacity of gD of *α*-herpesviruses to interact with a variety of receptors, including cell surface proteins of two different families and modified heparan sulfate, is astonishing. Why do these viruses use multiple receptors? Does it allow them to change their tropism in the course of an infection? Virus attachment to cells is normally mediated by gB and gC. However, gD is required for successful entry and is supposed to be involved in the activation of the fusogenic activity of the viral proteins gB and gH/gL. Wild-type strains of HSV-1 and -2 seem to be similar in the use of HveA or HveC for entry but they differ in the use of binding sites generated by sulfotransferases (3-OST-3) on heparan sulfate (Shukla *et al*., 1999). While the clinical manifestations of disease caused by the two serotypes are indistinguishable, there are differences in their epidemiology and pathogenesis (Corey & Spear, 1986*a*, *b*; Lafferty *et al*., 1987). HSV-1 is the usual cause of adult sporadic encephalitis, keratinitis and oral mucocutaneous lesions,

whereas HSV-2 is more likely to cause genital lesions, meningitis and neonatal infections. This could be influenced by their differential receptor usage determined by the capacity of HSV-1 to interact with 3-OST-3-modified heparan sulfate (Shukla *et al*., 1999).

As well as α-herpesviruses, interaction with heparan sulfate has been demonstrated for HIV-1 (Mondor *et al*., 1998), human cytomegalovirus (Compton *et al*., 1993), foot and mouth disease virus (Jackson *et al*., 1996), dengue virus (Chen *et al*., 1997), Sindbis virus (Byrnes & Griffin, 1998), vaccinia virus (Chung *et al*., 1998) and adeno-associated virus type 2 (Summerford & Samulski, 1998). It seems possible that heparan sulfate could help these viruses to adhere to a cell before further higher affinity receptors induce adhesion strengthening and mediate entry (Haywood, 1994). This model is supported by results obtained using the flaviviruses, dengue virus and TBEV. Dengue virus binds first to heparan sulfate and then to a high affinity receptor, which induces endocytosis and subsequent cell membrane fusion (Chen *et al*., 1997; Hung *et al*., 1999; Putnak *et al*., 1997). Thus, heparan sulfate proteoglycans on the cell surface can be used as initial attachment receptors by several viruses.

The tropism of the γ-herpesvirus Epstein–Barr virus is mediated by alternative usage of the complement receptor CD21 and an unknown receptor

Epstein–Barr virus (EBV) glycoproteins gp350/220 mediate the attachment of virus to cellular receptors. These heavily glycosylated envelope proteins are the product of a single EBV gene, which is expressed as alternatively spliced RNAs (Beisel *et al*., 1985). CD21, the human receptor for the complement protein C3dg, has been identified as a cellular receptor for EBV (Nemerow *et al*., 1986; Nemerow & Cooper, 1992; Tanner *et al*., 1987). CD21 is a single transmembrane protein of approximately 145 kDa containing 15 to 16 complement control protein (CCP) domains. The first two amino-terminal CCP domains of CD21 bear the virus-binding sites (Lowell *et al*., 1989). CD21 is expressed by B cells, follicular dendritic cells and a subset of thymocytes. Electron microscopic studies, as well as biochemical studies, have shown that EBV enters human peripheral blood B cells via large uncoated endocytic vesicles. In contrast to the entry pathway in primary B cells, EBV can directly fuse with the plasma membrane of target cells such as the B cell line Raji. Fusion is mediated by the EBV envelope protein gp85 (Nemerow & Cooper, 1992).

Interestingly, binding of EBV, or beads bearing the viral envelope proteins gp350/220, induce the capping and endocytosis of CD21 (Tanner *et al*., 1987; Tedder *et al*., 1986). Thus, as found for viruses such as HIV and measles virus (MV), infection of cells with EBV leads to the downregulation of its receptor, CD21, from the cell surface. The normal function of CD21 is not completely understood, but it certainly plays an important role in antigen-specific B cell activation and differentiation, processes which are disturbed by the interaction with EBV. After the binding of ligands, CD21 and the antigen receptor become associated in the B cell membrane. In addition, further cell surface molecules, such as CD19 and CD81, associate with CD21 and form a multimolecular complex, which is probably involved in signal transduction. Antigen localization and the generation of B memory cells are largely dependent on the presence of the complement protein C3, and soluble CD21 fragments can suppress the immune response in mice.

EBV, the causative agent of infectious mononucleosis, is closely associated with Burkitt's lymphoma and several benign and malignant lymphoproliferative diseases occurring in immunodeficient individuals. The cell tropism of EBV in these diseases can be explained by the use of CD21 as receptor. However, the EBV genome is also found in epithelial cell tumours such as nasopharyngeal and gastric carcinoma which do not express CD21. Therefore, the presence of a receptor other than CD21 on epitheloid gastric cells has been suggested (Hsu *et al*., 1996; Kasai *et al*., 1994; Kim *et al*., 1998; Yoshiyama *et al*., 1997). A very efficient mode of infection with EBV, much more efficient (up to 800-fold) than infection with cell-free virus, is direct cell-to-cell spread (Imai *et al*., 1998).

Measles virus: also more than one receptor

MV is a monotypic negative-strand RNA virus causing acute measles accompanied by a transient immunosuppression, acute post-infectious encephalomyelitis and CNS diseases based on MV persistence (for a review, see Griffin & Bellini, 1996). The envelope glycoproteins haemagglutinin (H), as a tetramer, and the fusion protein (F), probably as a trimer, interact with receptors on the target cell surface (Langedijk *et al*., 1997 and references therein). A complement regulatory protein containing four CCP domains, CD46, was identified as a receptor for vaccine strains of MV (for reviews, see Dörig *et al*., 1994; Gerlier *et al*., 1995). CD46 is expressed on almost all human cells except erythrocytes and cells in the CNS such as oligodendrocytes and a proportion of neurons and astrocytes (Johnstone *et al*., 1993; Ogata *et al*., 1997). Binding sites for MV H protein have been mapped to the first two extracellular CD46 domains (Buchholz *et al*., 1997; Casasnovas *et al*., 1999; Hsu *et al*., 1997, 1999; Manchester *et al*., 1997). MV infection of cells can result in the secretion of cytokines such as interferon-α/β, tumour necrosis factor-α, interleukin-1 and interleukin-6. Binding of MV to CD46 in the absence of infection can induce kinase-mediated signals in the contacted cells which contribute to the induction of cytokines (Ghali & Schneider-Schaulies, 1998; Wong *et al*., 1997). In the presence of interferon-γ, the synthesis of nitric oxide by macrophages is enhanced through the cytoplasmic domain of CD46 in response to MV infection (Hirano *et al*., 1999).

As in the case of EBV and HIV, MV can induce the downregulation of its receptor from the cell surface after infection or after the extracellular contact of cells with MV H protein (Krantic *et al*., 1995; Naniche *et al*., 1993; Schneider-Schaulies *et al*., 1996). Since the natural function of CD46 is to act as a cofactor for the cleavage of the complement factors C3b and C4b, and to protect cells from lysis by autologous complement (for a review, see Liszewski *et al*., 1991), CD46-modulation by MV enhances the sensitivity of cultured cells to complement (Schnorr *et al*., 1995). *In vivo*, this may cause a rapid clearing of infected cells and thus contribute to the attenuation of such downregulating MV strains. Different MV isolates vary considerably in their capacity to interact with CD46. In contrast to vaccine strains, a number of recent wild-type isolates do not downregulate CD46 (Schneider-Schaulies *et al*., 1995*a*, *b*). This capacity is closely related to amino acids at positions 451 and 481 in the H protein (Bartz *et al*., 1996; Lecouturier *et al*., 1996).

Recently, B cell lines have been used to isolate a number of MV strains which obviously do not interact with CD46 (Bartz *et al*., 1998; Hsu *et al*., 1998; Tanaka *et al*., 1998). MV isolates that do not interact with CD46 have a preferred tropism for lymphoid cells. Studies using recombinant MVs (Radecke *et al*., 1995) with defined envelope proteins have confirmed these findings (Johnston *et al*., 1999). It remains to be seen whether MVs present during the acute disease *in vivo* interact with CD46, and what consequences the differential receptor usage might have for the pathogenicity of acute and persistent MV infections.

The most intriguing question at present is how cellular receptors are involved in MV-induced immunosuppression. During immunosuppression, the number of peripheral blood lymphocytes is reduced and activated T cells are depleted from the circulation (Nanan *et al*., 1999; for reviews, see Griffin, 1995; Schneider-Schaulies & ter Meulen, 1999). *Ex vivo*, the proliferative response of peripheral blood lymphocytes to antigens or mitogens is strongly inhibited. The MV-induced immunosuppression is a multi-factorial process which may be influenced by soluble factors such as IL-12 (Karp *et al*., 1996) and the direct contact of the viral H–F glycoprotein complex and the surface of lymphocytes (Schlender *et al*., 1996). The contact requirements for the proliferative inhibition of lymphocytes have been defined by using recombinant viral glycoproteins and recombinant viruses, and CD46 appears not to be required (Niewiesk *et al*., 1997*a*; Schlender *et al*., 1996). Recent data indicate that although a native H–F complex is obligatory, the process of membrane fusion is not required for inhibition of T cell proliferation (Weidmann *et al*., 2000). As in the case of HIV gp41, cellular receptors involved in the proliferative inhibition of lymphocytes have not yet been identified.

MV-induced CNS diseases and the mechanisms supporting virus persistence have been studied extensively (for a review, see Schneider-Schaulies *et al*., 1999). The influence of the virus attachment protein H on neurovirulence was investigated using antibody escape mutants in rats (Liebert *et al*., 1994) and in a mouse model using a recombinant MV in which the H gene of the Edmonston strain was replaced by the H gene of the rodent-adapted neurovirulent MV strain CAM (Duprex *et al*., 1999*a*). After intracerebral injection into suckling mice only the recombinant virus bearing CAM-H, and not the virus with the Edmonston-H, induced a neurological disease. However, the neurovirulence of the recombinant virus was reduced compared to the wild-type CAM strain, indicating that other viral genes also contribute to CAM-induced pathogenicity.

Recently, CD46-transgenic mice have been used to define the role of the cellular receptor for the neurotropism and virulence of MV. In such animals the normally apathogenic Edmonston strain is able to cause widespread neuronal infection and death in neonates, and scattered infection of neurons of adult mice (Rall *et al*., 1997). These findings clearly demonstrate that expression of a suitable receptor on neurons can mediate neurovirulence. However, in the periphery of adult CD46-transgenic mice or rats, receptor expression did not lead to a significant increase of susceptibility for MV, suggesting an intracellular block of virus replication (Blixenkrone-Moller *et al*., 1998; Horvat *et al*., 1996; Niewiesk *et al*., 1997*b*). In contrast, a different line of CD46-transgenic mice seems to be more generally susceptible to MV infection (Oldstone *et al*., 1999). Clearly, these differences in the susceptibility of different CD46 transgenic mice need to be further investigated. In interferon-α/β-receptor-deficient mice expressing a CD46 transgene, intracerebral inoculation of adult animals with low doses of MV caused encephalitis (Mrkic *et al*., 1998). These findings underline the importance of the interferon system and associated intracellular factors for the virulence of this virus.

Receptor interactions of lymphocytic choriomeningitis virus (LCMV) strains determine pathogenesis

Infection of mice with LCMV has been extensively studied as a model system for virus persistence, immune-mediated pathology and immunosuppression (Borrow *et al*., 1995). LCMV is the prototype arenavirus with a single-stranded, ambisense RNA genome of two segments, 7220 and 3376 nucleotides, containing four open reading frames. The receptor-interacting envelope glycoprotein G is cleaved to an external G1 and a transmembrane G2 glycoprotein. LCMV enters rodent target cells via receptor-mediated endocytosis and pH-dependent fusion (Borrow & Oldstone, 1994). A cellular receptor for LCMV has recently been identified (Borrow & Oldstone, 1992; Cao *et al*., 1998 and references therein). Interestingly, several strains of LCMV and other arenaviruses, including Lassa, Oliveros and Mobala fever virus, bound to the same protein, namely α-dystroglycan. Dystroglycan is encoded by a single gene and processed into α- and β-chains, which form a complex. The dystroglycan complex is

expressed in a wide variety of tissues and cells, and mediates interactions of cells with the extracellular matrix.

Persistent infection of C3H/St mice with certain clones of LCMV strain WE can cause growth hormone deficiency syndrome (GHDS). Reassortant studies indicate that a single amino acid exchange at position 153 in the viral envelope protein G1 is sufficient to allow infection of the growth hormone-producing cells and cause GHDS (Teng *et al.*, 1996). It is not yet known whether this change in the virus tropism and pathogenicity is due to alterations in receptor usage of such clones. Another pair of LCMV strains, strain Armstrong and clone 13, have been found to cause differential immunosuppressive effects in mice (Borrow *et al.*, 1995). Mice infected with LCMV Armstrong rapidly clear the infection, whereas mice infected with clone 13 develop a generalized immunosuppression associated with loss of interdigitating dendritic cells and failure to stimulate the proliferation of T cells. These two strains differ in only two amino acids, at positions 260 in the G1 protein and 1079 in the RNA polymerase. A difference in the tropism of the two strains has been found, which is probably caused by a stronger binding affinity of clone 13 to the LCMV receptor. This could enable clone 13 to infect cells expressing limited amounts of α-dystroglycan, or to infect cells more effectively than the Armstrong strain. These findings suggest an association between receptor usage and pathogenicity.

Coronaviruses: receptors determine the host range

Coronaviruses are a group of enveloped, positive-strand RNA viruses. The closely related human coronavirus (HCV) 229E, porcine transmissible gastroenteritis virus (TGEV), feline infectious peritonitis virus (FIPV) and canine coronavirus (CCV) belong to serogroup 1 and are antigenically and genetically distinct from the so-called haemagglutinating coronaviruses, such as HCV-OC43, murine hepatitis virus (MHV) and bovine coronavirus (BCV), which belong to serogroup 2, and the avian infectious bronchitis virus (IBV), which comprises serogroup 3 (Table 1; for a review, see Siddell, 1995). The envelopes of all coronaviruses contain a spike protein (S), which binds to receptors on the target cell membrane. Some viruses in serogroup 2 have in addition a haemagglutinin esterase, which binds to cell membrane molecules bearing 9-*O*-acetylated neuraminic acid.

Coronaviruses of serogroup 1 interact species-specifically with aminopeptidase-N (APN) as the attachment receptor (Delmas *et al.*, 1992; Kolb *et al.*, 1996; Yeager *et al.*, 1992). APN is a type II transmembrane glycoprotein and belongs to the family of membrane-bound metallopeptidases (Ashmun *et al.*, 1992). The protein is found in large amounts on the microvillar membrane of the small intestine and is also present on renal proximal tubule epithelium, synaptic membranes of the CNS and cells of the granulocytic and monocytic lineage (Delmas *et al.*, 1994; Look *et al.*, 1989; Olsen *et al.*, 1988). Human APN (CD13) is used as a receptor by HCV 229E not only for infection of lung fibroblasts but also for infection of neuronal and glial tissue culture cells (Lachance *et al.*, 1998). Interestingly, the host range of coronaviruses is associated with receptor usage, while the disease type is not (Hegyi & Kolb, 1998; Tresnan & Holmes, 1998).

The receptor for MHV was initially identified as the biliary glycoprotein $Bgp1^a$, a member of the carcinoembryonic antigen (CEA) family of cell surface proteins (Dveksler *et al.*, 1991; Williams *et al.*, 1991). $Bgp1^a$ consists of four immunoglobulin-like extracellular domains, a transmembrane domain, and either a long or a short cytoplasmic tail. It is expressed at the sites of virus entry such as the apical membranes of respiratory and intestinal epithelial cell layers, the luminal surfaces of endothelial cells, on hepatocytes, B lymphocytes and macrophages (Coutelier *et al.*, 1994; Godfraind *et al.*, 1995). In the liver, $Bgp1^a$ expression correlates with infection of hepatocytes and endothelial cells, leading to the development of hepatitis. However, other cells expressing this molecule, such as endothelial cells of the CNS, are not infected (Godfraind & Coutelier, 1998). Although the molecular basis for this observation is not known, it may explain how the blood–brain barrier prevents dissemination of MHV A59 into the brain.

MHV A59 binds only to $Bgp1^a$ on intestinal brush border membranes of susceptible mice, and not to membranes from humans, cats, dogs, pigs, cows, rabbits, rats, cotton rats or chickens (Compton *et al.*, 1992). Other members of the CEA family in addition to $Bgp1^a$, namely $Bgp1^b$ (Dveksler *et al.*, 1993*a*, *b*; Yokomori & Lai, 1992), Bgp2 (Nedellec *et al.*, 1994) and brain CEA (Chen *et al.*, 1995) may also serve as receptors, with different binding efficiencies (Zelus *et al.*, 1998). $Bgp1^a$ is the major receptor for MHV in susceptible mice, whereas $Bgp1^b$, which is used less efficiently as a receptor, is expressed homozygously by resistant SJL mice (Williams *et al.*, 1990).

A change of receptor usage may be associated with the transition of the host range of coronaviruses from one species to the other. Conversely, experimental interspecies transfer of MHV also changed the receptor usage (Hensley *et al.*, 1998). The S protein of MHV has recently been exchanged by targeted RNA recombination for the S protein of FIPV (Kuo *et al.*, 2000). The resulting chimeric virus acquired the ability to infect feline cells and lost the ability to infect murine cells, supporting the view that the host range of coronavirus infections is mainly determined by receptor usage.

Do the known receptors for hepatitis viruses explain their liver tropism?

A cellular receptor for hepatitis A virus (HAV) has been identified by screening a cDNA expression library of African green monkey kidney cells with an infection-inhibiting antibody (Kaplan *et al.*, 1996). The HAV cellular receptor 1 (HAVcr-1) is a class I integral mucin-like membrane glycoprotein of unknown function (Kaplan *et al.*, 1996; Thompson

et al., 1998). As shown for other picornaviruses, low pH during the uptake of HAV by receptor-mediated endocytosis induces conformational changes in its capsid which may be the first step to uncoating the HAV genome (Bishop, 1999). huHAVcr-1 is expressed in all human organs, with higher levels in the kidney and testis (Feigelstock *et al*., 1998). Since extrahepatic sites of HAV replication were found in the gastrointestinal tract, liver, salivary glands, kidney, spleen and lymph nodes of experimentally infected primates, the liver-specific pathogenesis of HAV cannot easily be explained (Asher *et al*., 1995). The detection of HAV in various organs may correlate with the expression of HAVcr-1. However, it is likely that unknown co-receptors or intracellular factors are required to render cells fully susceptible to HAV infection.

Human hepatitis B virus (HBV), an enveloped hepadnavirus with a partially double-stranded DNA genome of approximately 3200 nucleotides in length, binds to a 50 kDa binding factor (HBV BF) present in serum and on the surface of cells (Budkowska *et al*., 1993). HBV BF is a neutral metalloproteinase which shares substrate specificity with a family of membrane-type matrix metalloproteinases. Treatment of HBV with the metalloproteinase results in cleavage of the N-terminal part of the pre-S2 envelope protein, and probably induces a conformational change in the pre-S1 domain that enables cell membrane attachment and virus entry into T lymphocytes (Budkowska *et al*., 1997). Since an inhibitor of the metalloproteinase blocked both processes, the host-dependent proteolytic activation of the envelope proteins seems to be essential for HBV entry into cells. The tissue tropism of HBV may be determined by this process of envelope activation and not by cellular receptors, which might be expressed ubiquitously (Budkowska *et al*., 1997; Köck *et al*., 1996).

An interesting mechanism has been proposed for the specific uptake of duck hepatitis B virus (DHBV) into hepatocytes using carboxypeptidase D (gp180) as a cellular receptor (Breiner *et al*., 1998; Kuroki *et al*., 1995; Tong *et al*., 1999; Urban *et al*., 1998). This peptidase is a Golgi-resident protein which is found only to a limited extent at the external cell surface. It cycles to and from the plasma membrane and in doing so, it may function as a carrier leading to the endocytosis of DHBV (Breiner *et al*., 1998). In spite of the high affinity binding of the DHBV surface protein to gp180, expression of gp180 in heterologous cells did not render them permissive to infection, suggesting that a species-specific co-receptor or co-factor is required for virus entry (Breiner *et al*., 1998). The highly specific infection of the liver by DHBV does not correlate with the ubiquitous gp180 expression, suggesting other mechanisms for targeting the virus to the liver.

Suramin, a polyanionic compound similar to heparin, was found to block HCV binding to human hepatoma cells at a concentration similar to that reported to be effective against dengue virus, suggesting an interaction of HCV with glycosaminoglycans on the cell surface (Chen *et al*., 1997; Garson *et al*., 1999). In addition, it was recently found that the E2 glycoprotein of HCV binds specifically to CD81, a transmembrane protein of the tetraspanin family (Pileri *et al*., 1998). It is not yet clear whether CD81 acts as a cellular receptor for attachment and entry of HCV into target cells. CD81 is involved in a number of biological responses including cell adhesion, proliferation and differentiation of T and B lymphocytes (Levy *et al*., 1998). Interestingly, the HCV E2 protein, after binding to CD81, induced aggregation of lymphoid cells and inhibited the proliferation of a B cell line (Flint *et al*., 1999). This might have important consequences for the pathogenesis of HCV. Since glycosaminoglycans and CD81 are expressed by a wide variety of cells, additional specific factors must determine the liver tropism of HCV.

Taken together, there is no obvious common receptor-mediated pathway for hepatic viruses and none of the cellular receptors known so far can explain the specific liver tropism and pathogenesis caused by these viruses. Interestingly, a receptor for Marburg virus, the asialoglycoprotein, is expressed specifically on liver cells, although this virus has a quite different tropism (Becker *et al*., 1995). Marburg and Ebola viruses infect a wide spectrum of cells including neutrophils, mononuclear cells, endothelial cells, fibroblasts and hepatocytes, and cause fulminant haemorrhagic fevers. Thus, this liver-specific receptor is used by a virus with a much broader tropism. The viral glycoprotein gene encodes three forms of the G protein: two secreted soluble forms, sGP and GP1, and the membrane bound GP1/2, which are involved in the virus-specific pathogenesis (for a review, see Klenk *et al*., 1998). The asialoglycoprotein receptor on hepatocytes may serve as a liver-specific receptor for Marburg virus, thereby explaining its liver tropism. However additional receptor molecules on other target cells must be postulated. The asialoglycoprotein receptor might be an attractive tool to target recombinant viruses as chemotherapeutic agents to the liver (Bitzer *et al*., 1997).

Cell-to-cell spread of viruses contributes to pathogenesis, but may not depend on cellular receptors

It was observed in the late 1960s that the MV ribonucleoprotein complex spreads in the CNS in the virtual absence of the viral envelope proteins and infectious particles. Cell-to-cell spread of MV was demonstrated *in vivo* and in tissue culture. It most likely involves localized fusion events at cell contact points, but CD46 is not required (Allen *et al*., 1996; Duprex *et al*., 1999*b*; Firsching *et al*., 1999; Lawrence *et al*., 2000; McQuaid *et al*., 1998; Meissner & Koschel, 1995; Urbanska *et al*., 1997). The velocity of virus spread also depends on the cytoplasmic parts of the viral glycoproteins and considerably contributes to pathogenesis (Cathomen *et al*., 1998*a*, *b*). In the case of canine distemper virus (CDV), another morbillivirus, antibodies to the cellular transmembrane molecule CD9 inhibit the CDV-induced formation of syncytia (cell–cell fusion), but not binding and uptake of virus (virus–cell

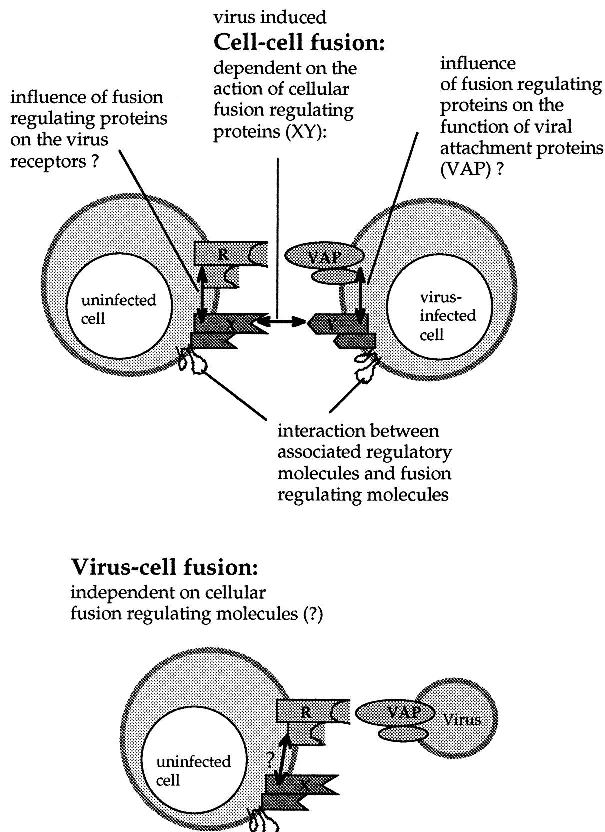

Fig. 2. Differences between cell–cell and virus–cell fusion. When an infected cell fuses with an uninfected cell, cellular surface molecules (XY) on both cells play a role in regulating the fusion, while in the case of virus–cell fusion, such molecules are not present on the virion.

fusion; Löffler *et al.*, 1997; Schmid *et al.*, 2000). In contrast, it has been demonstrated for feline immunodeficiency virus (FIV) that antibodies to CD9 block the assembly or release of the virus (De Parseval *et al.*, 1997; Willett *et al.*, 1997). Obviously cell-to-cell spread and the infection of cells with extracellular virus involve different mechanisms and different cell surface molecules, as hypothetically presented in Fig. 2.

The involvement of viral proteins in the infection of cells via exogenous virus particles in comparison to the cell-to-cell transmission is an important facet of the herpesvirus infection. The viral glycoproteins gE and gI of HSV play a role in cell-to-cell spread across junctions formed between fibroblasts and neurons, whereas mutants lacking both glycoproteins can infect fibroblasts as extracellular virus (Balam *et al.*, 1984; Dingwell *et al.*, 1994). In addition, the modification of glycoproteins with mannose-6-phosphate and mannose-6-phosphate receptors influences the virus plaque size (Brunetti *et al.*, 1995). Similar results have been described with another α-herpesvirus, pseudorabies virus (Karger *et al.*, 1998; Klupp *et al.*, 1999). These data show that the process by which HSV spreads from cell to cell is mechanistically different from virus entry into cells and requires the presence of different cellular receptor molecules.

The cellular fusion-regulating proteins (FRP)-1 and -2 play a role in cell–cell fusion. These proteins were initially found with monoclonal antibodies that stimulate the Newcastle disease virus (NDV)-induced cell–cell fusion (Ito *et al.*, 1987, 1992; Ohgimoto *et al.*, 1995). Interestingly, antibodies to FRP-1 stimulate NDV-induced and inhibit parainfluenza virus-induced cell fusion (Okamoto *et al.*, 1997). Recent data indicate that HIV-induced cell fusion is also regulated by FRP-1, integrins and the activation of tyrosine kinases (Ohta *et al.*, 1994; Tabata *et al.*, 1998). In addition, HIV DNA may also spread from cell to cell in a CD4-independent fashion via apoptotic bodies (Spetz *et al.*, 1999). Also, the syncytium formation of human T cell leukaemia virus type 1 is regulated in a cell-type-specific manner by ICAM-1, ICAM-3 and VCAM-1 and can be inhibited by antibodies to integrin β_2 or β_7 (Daenke *et al.*, 1999).

Conclusions

Infection of cells by cell-free virus and virus spread from cell to cell are different processes which may depend on the presence of different cellular surface molecules. In infected organs, the cell-to-cell spread contributes significantly to the pathogenesis of a viral disease. Underlying mechanisms are not well understood and require more research in the future. There are several viruses for which the host-specificity depends on their cellular receptors, whereas a specific organ or cell tropism appears often to be influenced by still unknown factors. Experiments are being undertaken to define the potential of certain viruses to change their host ranges. These are necessary steps in determining biosafety in xenotransplantation and gene therapy. Signal transduction as a consequence of a virus binding to its receptor is an important mechanism that influences virus cytopathogenicity and the immune response. A major impact on pathogenesis is due to the immunosuppressive capacity of many viruses which in part can also be exerted via cell surface receptor interactions. The increasing number of systems in which recombinant viruses can be applied will help to further investigate such virus–receptor interactions and to define the consequences of these interactions for tropism, virulence and pathogenesis.

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References

Agrez, M. V., Shafren, D. R., Gu, X., Cox, K., Sheppard, D. & Barry, R. D. (1997). Integrin αvβ6 enhances coxsackievirus B1 lytic infection of human colon cancer cells. *Virology* **239**, 71–77.

Aiken, C., Konner, J., Landau, N. R., Lenburg, M. E. & Trono, D. (1994). Nef induces CD4 endocytosis: requirement for a critical dileucine motif in the membrane-proximal CD4 cytoplasmic domain. *Cell* **76**, 853–864.

Allan, J. S., Strauss, J. & Buck, D. W. (1990). Enhancement of SIV infection with soluble receptor molecules. *Science* **247**, 1084–1088.

Allen, I. V., McQuaid, S., McMahon, J., Kirk, J. & McConnel, R. (1996). The significance of measles virus antigen and genome distribution in the CNS in SSPE for mechanisms of viral spread and demyelination. *Journal of Neuropathology & Experimental Neurology* **55**, 471–480.

Arita, M., Koike, S., Aoki, J., Horie, H. & Nomoto, A. (1998). Interaction of poliovirus with its purified receptor and conformational alteration in the virion. *Journal of Virology* **72**, 3578–3586.

Asher, L. V., Binn, L. N., Mensing, T. L., Marchwicki, R. H., Vassell, R. A. & Young, G. D. (1995). Pathogenesis of hepatitis A in orally inoculated owl monkeys (*Aotus trivirgatus*). *Journal of Medical Virology* **47**, 260–268.

Ashmun, R. A., Shapiro, L. H. & Look, A. T. (1992). Deletion of the zinc-binding motif of CD13/aminopeptidase N molecules results in loss of epitopes that mediate binding of inhibitory antibodies. *Blood* **79**, 3344–3349.

Baker, K. A., Dutch, R. E., Lamb, R. A. & Jardetzky, T. S. (1999). Structural basis for paramyxovirus-mediated membrane fusion. *Molecular Cell* **3**, 309–319.

Balam, P., Davis-Poynter, N., Bell, S., Atkinson, H., Browne, H. & Minson, T. (1984). An analysis of *in vitro* and *in vivo* phenotypes of mutants of herpes simplex virus type 1 lacking glycoproteins gG, gE, gI or the putative gJ. *Journal of General Virology* **75**, 1245–1258.

Bartz, R., Brinckmann, U., Dunster, L., Rima, B., ter Meulen, V. & Schneider-Schaulies, J. (1996). Mapping amino acids of the measles virus hemagglutinin responsible for receptor (CD46) downregulation. *Virology* **224**, 334–337.

Bartz, R., Firsching, R., Rima, B., ter Meulen, V. & Schneider-Schaulies, J. (1998). Differential receptor usage by measles virus strains. *Journal of General Virology* **79**, 1015–1025.

Becker, S., Spiess, M. & Klenk, H.-D. (1995). The asialoglycoprotein receptor is a potential liver-specific receptor for Marburg virus. *Journal of General Virology* **76**, 393–399.

Beisel, C., Tanner, J., Matsuo, T., Thorley-Lawson, D., Kezdy, F. & Kieff, E. (1985). Two major outer envelope glycoproteins of Epstein–Barr virus are encoded by the same gene. *Journal of Virology* **54**, 665–674.

Bergelson, J. M., Chen, M., Solomon, K. R., John, N. F., Lin, H. & Finberg, R. W. (1994). Decay accelerating factor (CD55), a glycosyl-phosphatidylinositol-anchored complement regulatory protein, is a receptor for several echoviruses. *Proceedings of the National Academy of Sciences, USA* **91**, 6245–6248.

Bergelson, J. M., Cunningham, J. A., Droguett, G., Kurt-Jones, E. A., Krithivas, A., Hong, J. S., Horwitz, M. S., Crowell, R. L. & Finberg, R. W. (1997). Isolation of a common receptor for coxsackie B viruses and adenoviruses 2 and 5. *Science* **275**, 1320–1323.

Berger, E. A., Murphy, P. M. & Farber, J. M. (1999). Chemokine receptors as HIV-1 coreceptors: roles in viral entry, tropism, and disease. *Annual Review of Immunology* **17**, 657–700.

Bernhardt, G., Bibb, J. A., Bradley, J. & Wimmer, E. (1994). Molecular characterization of the cellular receptor for poliovirus. *Virology* **199**, 105–110.

Bewley, M. C., Springer, K., Zhang, Y.-B., Freimuth, P. & Flanagan, J. M. (1999). Structural analysis of the mechanism of adenovirus binding to its human cellular receptor, CAR. *Science* **286**, 1579–1583.

Bhat, S., Spitalnid, S. L., Gonzalez-Scarano, F. & Silberberg, D. H. (1991). Galactosyl ceramide or a derivative is an essential component of the neural receptor for human immunodeficiency virus type 1 envelope glycoprotein gp120. *Proceedings of the National Academy of Sciences, USA* **88**, 7131–7134.

Bhat, S., Mettus, R. V., Reddy, E. P., Ugen, K. E., Srikanthan, V., Williams, W. V. & Weiner, D. B. (1993). The galactosyl ceramide/sulfatide receptor binding region of HIV-1 gp120 maps to amino acids 206–275. *AIDS Research and Human Retroviruses* **9**, 175–181.

Bishop, N. E. (1999). Conformational changes in the hepatitis A virus capsid in response to acidic conditions. *Journal of Medical Microbiology* **48**, 443–450.

Bitzer, M., Lauer, U., Baumann, C., Spiegel, M., Gregor, M. & Neubert, W. J. (1997). Sendai virus efficiently infects cells via the asialoglycoprotein receptor and requires the presence of cleaved F0 precursor proteins for this alternative route of cell entry. *Journal of Virology* **71**, 5481–5486.

Blixenkrone-Moller, M., Bernard, A., Bencsik, A., Sixt, N., Diamond, L. E., Logan, J. S. & Wild, T. F. (1998). Role of CD46 in measles virus infection in CD46 transgenic mice. *Virology* **249**, 238–248.

Borrow, P. & Oldstone, M. B. A. (1992). Characterization of lymphocytic choriomeningitis virus-binding protein(s): a candidate cellular receptor for the virus. *Journal of Virology* **66**, 7270–7281.

Borrow, P. & Oldstone, M. B. A. (1994). Mechanism of lymphocytic choriomeningitis virus entry into cells. *Virology* **198**, 1–9.

Borrow, P., Evans, C. F. & Oldstone, M. B. A. (1995). Virus-induced immunosuppression: immune system-mediated destruction of virus-infected dendritic cells results in generalized immune suppression. *Journal of Virology* **69**, 1059–1070.

Breiner, K. M., Urban, S. & Schaller, H. (1998). Carboxypeptidase D (gp180), a Golgi-resident protein, functions in the attachment and entry of avian hepatitis B viruses. *Journal of Virology* **72**, 8098–8104.

Brunetti, C. R., Burke, R. L., Hoflack, B., Ludwig, T., Dingwell, K. S. & Johnson, D. C. (1995). Role of mannose-6-phosphate receptors in herpes simplex virus entry into cells and cell-to-cell transmission. *Journal of Virology* **69**, 3517–3528.

Buchholz, C. J., Koller, D., Devaux, P., Mumenthaler, C., Schneider-Schaulies, J., Braun, W., Gerlier, D. & Cattaneo, R. (1997). Mapping of the primary binding site of measles virus to its receptor CD46. *Journal of Biological Chemistry* **272**, 22072–22079.

Budkowska, A., Quan, C., Groh, F., Bedossa, P., Dubreuil, P., Bouvet, J. P. & Pillot, J. (1993). Hepatitis B virus (HBV) binding factor in human serum: candidate for a soluble form of hepatocyte HBV receptor. *Journal of Virology* **67**, 4316–4322.

Budkowska, A., Maillard, P., Theret, N., Groh, F., Possehl, C., Topilko, A. & Crainic, R. (1997). Activation of the envelope proteins by a metalloproteinase enables attachment and entry of the hepatitis B virus into T-lymphocyte. *Virology* **237**, 10–22.

Byrnes, K. J. & Griffin, D. E. (1998). Binding of Sindbis virus to cell surface heparan sulfate. *Journal of Virology* **72**, 7349–7356.

Cao, W., Henry, M. D., Borrow, P., Yamada, H., Elder, J. H., Ravkov, E. V., Nichol, S. T., Compans, R., Campbell, K. P. & Oldstone, M. B. A. (1998). Identification of α-dystroglycan as a receptor for lymphocytic choriomeningitis virus and Lassa fever virus. *Science* **282**, 2079–2081.

Carr, C. M., Chaudhry, C. & Kim, P. S. (1997). Influenza hemagglutinin is spring-loaded by a metastable native conformation. *Proceedings of the National Academy of Sciences, USA* **94**, 14306–14313.

Casasnovas, J. M., Larvie, M. & Stehle, T. (1999). Crystal structure of two CD46 domains reveals an extended measles virus-binding surface. *EMBO Journal* **18**, 2911–2922.

Cathomen, T., Mrkic, B., Spehner, D., Drillien, R., Naef, R., Pavlovic, J., Aguzzi, A., Billeter, M. A. & Cattaneo, R. (1998*a*). A matrix-less measles virus is infectious and elicits extensive cell fusion: consequences for propagation in the brain. *EMBO Journal* **17**, 3899–3908.

Cathomen, T., Naim, H. Y. & Cattaneo, R. (1998*b*). Measles viruses with altered envelope protein cytoplasmic tails gain cell fusion competence. *Journal of Virology* **72**, 1224–1234.

Chapman, M. S. & Rossman, M. G. (1993). Comparison of the surface properties of picornaviruses: strategies for hiding the receptor site from immune surveillance. *Virology* **195**, 745–752.

Chen, D. S., Asanaka, M., Yokomori, K., Wang, F., Hwang, S. B., Li, H. P. & Lai, M. M. (1995). A pregnancy-specific glycoprotein is expressed in the brain and serves as a receptor for mouse hepatitis virus. *Proceedings of the National Academy of Sciences, USA* **92**, 12095–12099.

Chen, Y., Maguire, T., Hileman, R. E., Fromm, J. R., Esko, J. D., Linhardt, R. J. & Marks, R. M. (1997). Dengue virus infectivity depends on envelope protein binding to target cell heparan sulfate. *Nature Medicine* **3**, 866–871.

Chiu, C. Y., Mathias, P., Nemerow, G. R. & Stewart, P. L. (1999). Structure of adenovirus complexed with its internalization receptor, $\alpha v\beta 5$ integrin. *Journal of Virology* **73**, 6759–6768.

Chung, C. S., Hsiao, J. C., Chang, Y. S. & Chang, W. (1998). A27L protein mediates vaccinia virus interaction with cell surface heparan sulfate. *Journal of Virology* **72**, 1577–1585.

Colston, W. & Racaniello, V. R. (1994). Soluble receptor-resistant poliovirus mutants identify surface and internal capsid residues that control interaction with the cell receptor. *EMBO Journal* **13**, 5855–5862.

Compans, R. W. (1995). Virus entry and release in polarized epithelial cells**.** *Current Topics in Microbiology and Immunology* **202**, 209–219.

Compton, S. R., Stephensen, C. B., Snyder, S. W., Weismiller, D. G. & Holmes, K. V. (1992). Coronavirus species specificity: murine coronavirus binds to a mouse-specific epitope on its carcinoembryonic antigen-related receptor glycoprotein. *Journal of Virology* **66**, 7420–7428.

Compton, T., Nowlin, D. M. & Cooper, N. R. (1993). Initiation of human cytomegalovirus infection requires initial interaction with cell surface heparan sulfate. *Virology* **193**, 834–841.

Corey, L. & Spear, P. G. (1986*a*). Infections with herpes simplex viruses (1). *New England Journal of Medicine* **314**, 686–691.

Corey, L. & Spear, P. G. (1986*b*). Infections with herpes simplex viruses (2). *New England Journal of Medicine* **314**, 749–757.

Coutelier, J.-P., Godfraind, C., Dveksler, G. S., Wysocka, M., Cardellichio, H., Noel, H. & Holmes, K. V. (1994). B lymphocyte and macrophage expression of carcinoembryonic antigen-related adhesion molecules that serve as receptors for murine coronavirus. *European Journal of Immunology* **24**, 1383–1390.

Daenke, S., McCracken, S. A. & Booth, S. (1999). Human T-cell leukaemia/lymphoma virus type 1 syncytium formation is regulated in a cell-specific manner by ICAM-1, ICAM-3 and VCAM-1 and can be inhibited by antibodies to integrin β_2 or β_7. *Journal of General Virology* **80**, 1429–1436.

Deatly, A. M., Coleman, J. W., McMullen, G., McAuliffe, M., Jayarama, V., Cupo, A., Crowley, J. C., McWilliams, T. & Taffs, R. E. (1999). Poliomyelitis in intraspinally inoculated poliovirus receptor transgenic mice. *Virology* **255**, 221–227.

Delmas, B., Gelfi, J., L'Haridon, R., Vogel, L. K., Sjostrom, H., Noren, O. & Laude, H. (1992). Aminopeptidase N is a major receptor for the entero-pathogenic coronavirus TGEV. *Nature* **357**, 417–420.

Delmas, B., Gelfi, J., Kut, E., Syostrom, H., Noren, O. & Laude, H. (1994). Determinants essential for the transmissible gastroenteritis virus-receptor interaction reside within a domain of aminopeptidase-N that is distinct from the enzymatic site. *Journal of Virology* **68**, 5216–5224.

Denner, J. (1998). Immunosuppression by retroviruses: implications for xenotransplantation. *Xenotransplantation* **862**, 75–86.

De Parseval, A., Lerner, D. L., Borrow, P., Willett, B. J. & Elder, J. H. (1997). Blocking of feline immunodeficiency virus infection by a monoclonal antibody to CD9 is via inhibition of virus release rather than interference with receptor binding. *Journal of Virology* **71**, 5742–5749.

Dingwell, K. S., Brunetti, C. R., Hendricks, R. L., Tang, Q., Tang, M., Rainbow, A. J. & Johnson, D. C. (1994). Herpes simplex virus glycoproteins E and I facilitate cell-to-cell spread in vivo and across junctions of cultured cells. *Journal of Virology* **68**, 834–845.

Dörig, R. E., Marcil, A. & Richardson, C. D. (1994). CD46, a primate-specific receptor for measles virus. *Trends in Microbiology* **2**, 312–318.

Dove, A. W. & Racaniello, V. R. (1997). Cold-adapted poliovirus mutants bypass a post entry replication block. *Journal of Virology* **71**, 4728–4735.

Duprex, W. P., Duffy, I., McQuaid, S., Hamill, L., Cosby, S. L., Billeter, M. A., Schneider-Schaulies, J., ter Meulen, V. & Rima, B. K. (1999*a*). The H gene of rodent brain-adapted measles virus confers neurovirulence to the Edmonston vaccine strain. *Journal of Virology* **73**, 6916–6922.

Duprex, W. P., McQuaid, S., Hangartner, L., Billeter, M. A. & Rima, B. K. (1999*b*). Observation of measles virus cell-to-cell spread in astrocytoma cells by using a green fluorescent protein-expressing recombinant virus. *Journal of Virology* **73**, 9568–9575.

Dveksler, G. S., Pensiero, M. N., Cardellichio, C. B., Williams, R. K., Jiang, G. S., Holmes, K. V. & Dieffenbach, C. W. (1991). Cloning of the mouse hepatitis virus (MHV) receptor: expression in human and hamster cell lines confers susceptibility to MHV. *Journal of Virology* **65**, 6881–6891.

Dveksler, G. S., Dieffenbach, C. W., Cardellichio, C. B., McCuaig, K., Pensiero, M. N., Jiang, G. S., Beauchemin, N. & Holmes, K. V. (1993*a*). Several members of the mouse carcinoembryonic antigen-related glycoprotein family are functional receptors for the coronavirus mouse hepatitis virus A59. *Journal of Virology* **67**, 1–8.

Dveksler, G. S., Pensiero, M. N., Dieffenbach, C. W., Cardellichio, C. B., Basile, A. A., Elia, P. E. & Holmes, K. V. (1993*b*). Mouse hepatitis virus strain A59 and blocking antireceptor monoclonal antibody bind to the N-terminal domain of cellular receptor. *Proceedings of the National Academy of Sciences, USA* **90**, 1716–1720.

Eckert, D. M., Malashkevich, V. N., Hong, L. H., Carr, P. A. & Kim, P. S. (1999). Inhibiting HIV-1 entry: discovery of D-peptide inhibitors that target the gp41 coiled-coil pocket. *Cell* **99**, 103–115.

Fauci, A. S. (1993). Multifactorial nature of human immunodeficiency virus disease: implications for therapy. *Science* **262**, 1011–1018.

Fauci, A. S. (1996). Host factors and the pathogenesis of HIV-induced disease. *Nature* **384**, 529–534.

Feigelstock, D., Thompson, P., Mattoo, P., Zhang, Y. & Kaplan, G. G. (1998). The human homolog of HAVcr-1 codes for a hepatitis A virus cellular receptor. *Journal of Virology* **72**, 6621–6628.

Firsching, R., Buchholz, C. J., Schneider, U., Cattaneo, R., ter Meulen, V. & Schneider-Schaulies, J. (1999). Measles virus spread by cell-cell contacts: uncoupling of contact-mediated receptor (CD46) down-regulation from virus uptake. *Journal of Virology* **73**, 5265–5273.

Flint, M., Maidens, C., Loomis-Price, L. D., Shotton, C., Dubuisson, J., Monk, P., Higginbottom, A., Levy, S. & McKeating, J. A. (1999). Characterization of hepatitis C virus E2 glycoprotein interaction with a putative cellular receptor, CD81. *Journal of Virology* **73**, 6235–6244.

Freistadt, M. S. (1994). Distribution of the poliovirus receptor in human tissue. In *Cellular Receptors for Animal Viruses*, pp. 445–462. Edited by E. Wimmer. Cold Spring Harbour, NY: Cold Spring Harbour Laboratory Press.

Freistadt, M. S., Fleit, H. B. & Wimmer, E. (1993). Poliovirus receptor

on human blood cells: a possible extraneural site of poliovirus replication. *Virology* **195**, 798–803.

Garson, J. A., Lubach, D., Passas, J., Whitby, K. & Grant, P. R. (1999). Suramin blocks hepatitis C binding to human cells in vitro. *Journal of Medical Virology* **57**, 238–242.

Geraghty, R. J., Krumenacher, C., Cohen, G. H., Eisenberg, R. J. & Spear, P. G. (1998). Entry of alphaherpesviruses mediated by poliovirus receptor-related protein 1 and poliovirus receptor. *Science* **280**, 1618–1620.

Gerlier, D., Varior-Krishnan, G. & Devaux, P. (1995). CD46-mediated measles virus entry: a first key to host-range specificity. *Trends in Microbiology* **3**, 338–345.

Ghali, M. & Schneider-Schaulies, J. (1998). Receptor (CD46)- and replication-mediated interleukin-6 induction by measles virus in human astrocytoma cells. *Journal of Neurovirology* **4**, 521–530.

Godfraind, C. & Coutelier, J. P. (1998). Morphological analysis of mouse hepatitis virus A59-induced pathology with regard to viral receptor expression. *Histology and Histopathology* **13**, 181–199.

Godfraind, C., Langreth, S. G., Cardellichio, C. B., Knobler, R., Coutelier, J. P., Dubois-Dalcq, M. & Holmes, K. V. (1995). Tissue and cellular distribution of an adhesion molecule in the carcinoembryonic antigen family that serves as a receptor for mouse hepatitis virus. *Laboratory Investigation* **73**, 615–627.

Griffin, D. E. (1995). Immune responses during measles virus infection. *Current Topics of Microbiology and Immunology* **191**, 117–134.

Griffin, D. E. & Bellini, W. J. (1996). Measles virus. In *Fields Virology*, 3rd edn, pp. 1267–1312. Edited by B. N. Fields, D. M. Knipe & P. M. Howley. Philadelphia: Lippincott–Raven.

Gromeier, M., Bossert, B., Arita, M., Nomoto, A. & Wimmer, E. (1999). Dual stem loops within the poliovirus internal entry site control neurovirulence. *Journal of Virology* **73**, 958–964.

Haraguchi, S., Good, R. A. & Day, N. K. (1995). Immunosuppressive retroviral peptides: cAMP and cytokin patterns. *Immunology Today* **16**, 595–603.

Harouse, J. M., Laughlin, M. A., Pletcher, C., Friedman, H. M. & Gonzalez-Scarano, F. (1991). Entry of human immunodeficiency virus-1 into glial cells proceeds via an alternative, efficient pathway. *Journal of Leukocyte Biology* **49**, 605–609.

Haywood, A. M. (1994). Virus receptors: binding, adhesion strengthening, and changes in viral structure. *Journal of Virology* **68**, 1–5.

Hegyi, A. & Kolb, A. F. (1998). Characterization of determinants involved in the feline infectious peritonitis virus receptor function of feline aminopeptidase N. *Journal of General Virology* **79**, 1387–1391.

Hensley, L. E., Holmes, K. V., Beauchemin, N. & Baric, R. S. (1998). Virus–receptor interactions and interspecies transfer of a mouse hepatitis virus. *Advances in Experimental Medicine and Biology* **440**, 33–41.

Herbein, G., Mahlknecht, U., Batliwalla, F., Gregersen, P., Pappas, T., Butler, J., O'Brien, W. A. & Verdin, E. (1998). Apoptosis of CD8+ T cells is mediated by macrophages through interaction of HIV gp120 with chemokine receptor CXCR4. *Nature* **395**, 189–194.

Hirano, A., Yang, Z., Katayama, Y., Korte-Sarfaty, J. & Wong, T. C. (1999). Human CD46 enhances nitric oxide production in mouse macrophages in response to measles virus infection in the presence of gamma interferon: dependence on the CD46 cytoplasmic domains. *Journal of Virology* **73**, 4776–4785.

Hladik, F., Lentz, G., Akridge, R. E., Peterson, G., Kelley, H., McElroy, A. & McElrath, M. J. (1999). Dendritic cell–T cell interactions support coreceptor-independent human immunodeficiency virus type 1 transmission in the human genital tract. *Journal of Virology* **73**, 5833–5842.

Horvat, B., Rivailler, P., Varior-Krishnan, G., Cardoso, A., Gerlier, D. & Rabourdin-Combe, C. (1996). Transgenic mice expressing human measles virus (MV) receptor CD46 provide cells exhibiting different permissivities to MV infections. *Journal of Virology* **70**, 6673–6681.

Hsu, H. C., Chen, C. C., Huang, G. T. & Lee, P. H. (1996). Clonal Epstein–Barr virus associated cholangiocarcinoma with lympho-epithelioma-like component. *Human Pathology* **27**, 848–850.

Hsu, E. C., Dörig, R., Sarangi, F., Marcil, A., Iorio, C. & Richardson, C. D. (1997). Artificial mutations and natural variations in the CD46 molecules from human and monkey cells define regions important for measles virus binding. *Journal of Virology* **71**, 6144–6154.

Hsu, E. C., Sarangi, F., Iorio, C., Sidhu, M. S., Udem, S. A., Dillehay, D. L., Xu, W., Rota, P., Bellini, W. J. & Richardson, C. D. (1998). A single amino acid change in the hemagglutinin protein of measles virus determines its ability to bind CD46 and reveals another receptor on marmoset B cells. *Journal of Virology* **72**, 2905–2916.

Hsu, E. C., Sabatinos, S., Hoedemaeker, F. J., Rose, D. R. & Richardson, C. D. (1999). Use of site-specific mutagenesis and monoclonal antibodies to map regions of CD46 that interact with measles virus H protein. *Virology* **258**, 314–326.

Huang, S., Kamata, T., Takada, Y., Ruggeri, Z. M. & Nemerow, G. R. (1996*a*). Adenovirus interaction with distinct integrins mediate separate events in cell entry and gene delivery to hematopoietic cells. *Journal of Virology* **70**, 4502–4508.

Huang, Y. X., Paxton, W. A., Wolinsky, S. M., Neumann, A. U., Zhang, L. Q., Yazdanbakhsh, K., Kunstman, K., Erickson, D., Dragon, E., Landau, N. R., Phair, J., Ho, D. D. & Koup, R. A. (1996*b*). The role of a mutant CCR5 allele in HIV-1 transmission and disease progression. *Nature Medicine* **2**, 1240–1243.

Hung, S.-H., Lee, P.-L., Chen, H.-W., Chen, L.-K., Kao, C.-L. & King, C.-C. (1999). Analysis of the steps involved in dengue virus entry into host cells. *Virology* **257**, 156–167.

Imai, S., Nishikawa, J. & Takada, K. (1998). Cell-to-cell contact as an efficient mode of Epstein–Barr virus infection of diverse human epithelial cells. *Journal of Virology* **72**, 4371–4378.

Immergluck, L. C., Domowicz, M. S., Schwartz, N. B. & Herold, B. C. (1998). Viral and cellular requirements for entry of herpes simplex virus type 1 into primary neuronal cells. *Journal of General Virology* **79**, 549–559.

Ito, Y., Tsurudome, M., Yamada, A. & Hishiyama, M. (1987). Induction of cell fusion in Newcastle disease virus-infected L929 cells by anti-L929 cell antisera. *Journal of General Virology* **68**, 1261–1266.

Ito, Y., Komada, H., Kusagawa, S., Tsurudome, M., Matsumara, H., Kawano, M., Ohta, H. & Nishio, M. (1992). Fusion regulation proteins on the cell surface: isolation and characterization of monoclonal antibodies which enhance giant polykarocyte formation in Newcastle disease virus-infected cell lines of human origin. *Journal of Virology* **66**, 5999–6007.

Jabbar, M. A. & Nayak, D. P. (1990). Intracellular interaction of human immunodeficiency virus type 1 (ARV-2) envelope glycoprotein gp160 with CD4 blocks the movement and maturation of CD4 to the plasma membrane. *Journal of Virology* **64**, 6297–6304.

Jackson, T., Ellard, F. M., Ghazaleh, R. A., Brookes, S. M., Blakemore, W. E., Cortyn, A. H., Stuart, D. I., Newman, J. W. & King, A. M. (1996). Efficient infection of cells in culture by type O foot and mouth disease virus requires binding to cell surface heparan sulfate. *Journal of Virology* **70**, 5282–5287.

Johnston, I. C. D., ter Meulen, V., Schneider-Schaulies, J. & Schneider-Schaulies, S. (1999). A recombinant measles vaccine virus expressing

wild-type glycoproteins: consequences for viral spread and cell tropism. *Journal of Virology* **73**, 6903–6915.

Johnstone, R. W., Loveland, B. E. & McKenzie, I. F. C. (1993). Identification and quantification of complement regulator CD46 on normal human tissues. *Immunology* **79**, 341–347.

Kaplan, G., Peters, D. & Racaniello, V. R. (1990). Poliovirus mutants resistant to neutralization with soluble cell receptors. *Science* **250**, 1596–1599.

Kaplan, G., Totsuka, A., Thompson, P., Akatsuka, T., Moritsugu, Y. & Feinstone, S. M. (1996). Identification of a surface protein on African green monkey kidney cells as a receptor for hepatitis A virus. *EMBO Journal* **15**, 4282–4296.

Karger, A., Schmidt, J. & Mettenleiter, T. C. (1998). Infectivity of a pseudorabies virus mutant lacking attachment glycoproteins C and D. *Journal of Virology* **72**, 7341–7348.

Karp, C. L., Wysocka, M., Wahl, L. M., Ahearn, J. M., Cuomo, P. J., Sherry, B., Trinchieri, G. & Griffin, D. E. (1996). Mechanism of suppression of cell-mediated immunity by measles virus. *Science* **273**, 228–231.

Kasai, K., Sato, Y., Kameya, T., Inoue, H., Yoshimura, H., Kon, S. & Kikuchi, K. (1994). Incidence of latent infection of Epstein–Barr virus in lung cancers – an analysis of EBER1 expression in lung cancers by in situ hybridization. *Journal of Pathology* **174**, 257–265.

Kim, Y. S., Paik, S. R., Kim, H. K., Yeom, B. W., Kim, I. & Lee, D. (1998). Epstein–Barr virus and CD21 expression in gastrointestinal tumors. *Pathology Research and Practice* **194**, 705–711.

Klatzmann, D., Champagne, E., Chamaret, S., Gruest, J., Guetard, D., Hercend, T., Gluckman, J.-C. & Montagnier, L. (1984). T-lymphocyte T4 molecule behaves as the receptor for human retrovirus LAV. *Nature* **312**, 767–768.

Klenk, H.-D., Volchkov, V. E. & Feldmann, H. (1998). Two strings to the bow of Ebola virus. *Nature Medicine* **4**, 388–389.

Klupp, B. G. & Mettenleiter, T. C. (1999). Glycoprotein gL-independent infectivity of pseudorabies virus is mediated by a gD–gH fusion protein. *Journal of Virology* **73**, 3014–3022.

Knight, S. C. & Patterson, S. (1997). Bone marrow-derived dendritic cells, infection with human immunodeficiency virus, and immunopathology. *Annual Review of Immunology* **15**, 593–615.

Köck, J., Theilemann, L., Galle, P. & Schlicht, H.-J. (1996). Hepatitis B virus nucleic acid associated with human peripheral blood mononuclear cells do not originate from replicating virus. *Hepatology* **23**, 405–413.

Koike, S., Horie, H., Ise, I., Okitsu, A., Yoshida, M., Iizuka, N., Takeuchi, K., Tagegami, T. & Nomoto, A. (1990). The poliovirus receptor protein is produced both as membrane-bound and secreted forms. *EMBO Journal* **9**, 3217–3222.

Koike, S., Taya, C., Kurata, T., Abe, S., Ise, I., Yonekawa, H. & Nomoto, A. (1991). Transgenic mice susceptible to poliovirus. *Proceedings of the National Academy of Sciences, USA* **88**, 951–955.

Kolb, A. F., Maile, J., Heister, A. & Siddell, S. G. (1996). Characterization of functional domains in the human coronavirus HCV 229E receptor. *Journal of General Virology* **77**, 2515–2521.

Krantic, S., Gimenez, C. & Rabourdin-Combe, C. (1995). Cell-to-cell contact via measles virus haemagglutinin–CD46 interaction triggers CD46 downregulation. *Journal of General Virology* **76**, 2793–2800.

Kuhn, R. J. (1997). Identification and biology of cellular receptors for the coxsackie B viruses group. *Current Topics in Microbiology and Immunology* **223**, 209–226.

Kuo, L., Godeke, G.-J., Raamsman, M. J. B., Masters, P. S. & Rottier, P. J. M. (2000). Retargeting of coronavirus by substitution of the spike glycoprotein ectodomain: crossing the host cell species barrier. *Journal of Virology* **74**, 1393–1406.

Kuroki, K., Eng, F., Ishikawa, T., Turck, C., Harada, F. & Ganem, D. (1995). Gp180, a host cell glycoprotein that binds duck hepatitis B virus particles, is encoded by a member of the carboxypeptidase gene family. *Journal of Biological Chemistry* **270**, 15022–15028.

Lachance, C., Arbour, N., Cashman, N. R. & Talbot, P. J. (1998). Involvement of aminopeptidase N (CD13) in infection of human neural cells by human coronavirus 229E. *Journal of Virology* **72**, 6511–6519.

Lafferty, W. E., Coombs, R. W., Benedetti, J., Critchlow, C. & Corey, L. (1987). Recurrences after oral and genital herpes simplex virus infection. Influences of site of infection and viral type. *New England Journal of Medicine* **316**, 1444–1449.

Langedijk, J. P. M., Daus, F. J. & van Oirschot, J. T. (1997). Sequence and structure alignment of paramyxoviridae attachment proteins and discovery of enzymatic activity for a morbillivirus hemagglutinin. *Journal of Virology* **71**, 6155–6167.

Lawrence, D. M. P., Patterson, C. E., Gales, T. L., D'Orazio, J. L., Vaughn, M. M. & Rall, G. F. (2000). Measles virus spread between neurons requires cell contact but not CD46 expression, syncytium formation, or extracellular virus production. *Journal of Virology* **74**, 1908–1918.

Lecouturier, V., Fayolle, J., Caballero, M., Carabana, J., Celma, M. L., Fernandez-Munoz, R., Wild, T. F. & Buckland, R. (1996). Identification of two amino acids in the hemagglutinin glycoprotein of measles virus (MV) that govern hemadsorption, HeLa cell fusion, and CD46 downregulation: phenotypic markers that differentiate vaccine and wild-type MV strains. *Journal of Virology* **70**, 4200–4204.

Leon-Monzon, M. E., Illa, I. & Dalakas, M. C. (1995). Expression of poliovirus receptor in human spinal cord and muscle. *Annals of the New York Academy of Sciences* **753**, 48–57.

Levy, S., Todd, S. C. & Maecker, H. T. (1998). CD81 (TAPA-1): a molecule involved in signal transduction and cell adhesion in the immune system. *Annual Review of Immunology* **16**, 89–109.

Liao, S. & Racaniello, V. R. (1997). Allele-specific adaptation of poliovirus VP1 B-C loop variants to mutant cell receptors. *Journal of Virology* **71**, 9770–9777.

Liebert, U. G., Flanagan, S. G., Löffler, S., Baczko, K., ter Meulen, V. & Rima, B. (1994). Antigenic determinants of measles virus hemagglutinin associated with neurovirulence. *Journal of Virology* **68**, 1486–1493.

Libert, F., Cochaux, P., Beckman, G., Samson, M., Aksenova, M., Cao, A., Czeizel, A., Claustres, M., de la Rua, C., Ferrari, M., Ferrec, C., Glover, G., Grinde, B., Guran, S., Kucinskas, V., Lavinha, J., Mercier, B., Ogur, G., Peltonen, L., Rosatelli, C., Schwartz, M., Spitsyn, V., Timar, L., Beckman, L., Parmentier, M. & Vassart, G. (1998). The delta CCR5 mutation conferring protection against HIV-1 in Caucasian populations has a single and recent origin in Northeastern Europe. *Human Molecular Genetics* **7**, 399–406.

Liszewski, M. K., Post, T. W. & Atkinson, J. P. (1991). Membrane cofactor protein (MCP or CD46): newest member of the regulators of complement activation gene cluster. *Annual Review of Immunology* **9**, 431–455.

Liu, R., Paxton, W. A., Choe, S., Ceradini, D., Martin, S. R., Horuk, R., Macdonald, M. E., Stuhlmann, H., Koup, R. A. & Landau, N. R. (1996). Homozygous defect in HIV coreceptor accounts for resistance of some multiply-exposed individuals to HIV-1 infection. *Cell* **86**, 367–377.

Löffler, S., Lottspeich, F., Lanza, F., Azorsa, D. O., ter Meulen, V. & Schneider-Schaulies, J. (1997). CD9, a tetraspan transmembrane protein, renders cells susceptible to canine distemper virus. *Journal of Virology* **71**, 42–49.

Look, A. T., Ashmun, R. A., Shapiro, L. H. & Peiper, S. C. (1989). Human myeloid plasma membrane glycoprotein CD13 (gp150) is identical to aminopeptidase N. *Journal of Clinical Investigation* **83**, 1299–1307.

Lowell, C. A., Klickstein, L. B., Carter, R. H., Mitchell, J. A., Fearon, D. T. & Ahearn, J. M. (1989). Mapping the Epstein–Barr virus and C3dg binding sites to a common domain on complement receptor type 2. *Journal of Experimental Medicine* **170**, 1931–1946.

Macadam, A. J., Pollard, S. R., Ferguson, G., Dunn, G., Skuce, R., Almond, J. W. & Minor, P. D. (1993). Genetic bases of attenuation of the Sabin type 2 vaccine strain of poliovirus in primates. *Virology* **192**, 18–26.

McQuaid, S., Campbell, S., Wallace, I. J. C., Kirk, J. & Cosby, S. L. (1998). Measles virus infection and replication in undifferentiated and differentiated human neuronal cells in culture. *Journal of Virology* **72**, 5245–5250.

Manchester, M., Gairin, J. E., Patterson, J. B., Alvarez, J., Liszewski, M. K., Eto, D. S., Atkinson, J. P. & Oldstone, M. B. A. (1997). Measles virus recognizes its receptor, CD46, via two distinct binding domains within SCR 1–2. *Virology* **233**, 174–184.

Mebatsion, T., Finke, S., Weiland, F. & Conzelmann, K.-K. (1997). A CXCR4/CD4 pseudotype rhabdovirus that selectively infects HIV-1 envelope protein-expressing cells. *Cell* **90**, 841–847.

Meissner, N. & Koschel, K. (1995). Downregulation of endothelin receptor mRNA synthesis in C6 rat astrocytoma cells by persistent measles virus and canine distemper virus infections. *Journal of Virology* **69**, 5191–5194.

Mendelsohn, C. L., Wimmer, E. & Racaniello, V. R. (1989). Cellular receptor for poliovirus: molecular cloning, nucleotide sequence, and expression of a new member of the immunoglobulin superfamily. *Cell* **56**, 855–862.

Milone, M. C. & Fitzgerald-Bocarsly, P. (1998). The mannose receptor mediates induction of IFN-α in peripheral blood dendritic cells by enveloped RNA and DNA viruses. *Journal of Immunology* **162**, 2391–2399.

Mondor, I., Ugolini, S. & Sattentau, Q. J. (1998). Human immunodeficiency virus type 1 attachment to HeLa CD4 cells is CD4 independent and gp120 dependent and requires cell surface heparans. *Journal of Virology* **72**, 3623–3634.

Montgomery, R. I., Warner, M. S., Lum, B. J. & Spear, P. G. (1996). Herpes simplex virus-1 entry into cells mediated by a novel member of the TNF/NGF receptor family. *Cell* **87**, 427–436.

Mrkic, B., Pavlovic, J., Rulicke, T., Volpe, P., Buchholz, C. J., Hourcade, D., Atkinson, J. P., Aguzzi, A. & Cattaneo, R. (1998). Measles virus spread and pathogenesis in genetically modified mice. *Journal of Virology* **72**, 7420–7427.

Nanan, R., Chittka, B., Hadam, M. & Kreth, H. W. (1999). Measles virus infection causes transient depletion of activated T cells from peripheral circulation. *Journal of Clinical Virology* **12**, 201–210.

Naniche, D., Wild, T. F., Rabourdin-Combe, C. & Gerlier, D. (1993). Measles virus haemagglutinin induces down-regulation of gp57/67, a molecule involved in virus binding. *Journal of General Virology* **74**, 1073–1079.

Nedellec, P., Dveksler, G. S., Daniels, E., Turbide, C., Chow, B., Basile, A. A., Holmes, K. V. & Beauchemin, N. (1994). Bgp2, a new member of the carcinoembryonic antigen-related gene family, encodes an alternative receptor for mouse hepatitis viruses. *Journal of Virology* **68**, 4525–4537.

Nemerow, G. R. & Cooper, N. R. (1992). CR2 (CD21) mediated infection of B lymphocytes by Epstein–Barr virus. *Seminars in Virology* **3**, 117–124.

Nemerow, G. R., Siaw, M. F. E. & Cooper, N. R. (1986). Purification of the Epstein–Barr virus/C3d complement receptor of human B lymphocytes: antigenic and functional properties of the purified protein. *Journal of Virology* **58**, 709–712.

Niewiesk, S., Eisenhuth, I., Fooks, A., Clegg, C. S., Schnorr, J.-J., Schneider-Schaulies, S. & ter Meulen, V. (1997 *a*). Measles virus-induced immune suppression in the cotton rat (*Sigmodon hispidus*) model depends on viral glycoproteins. *Journal of Virology* **71**, 7214–7219.

Niewiesk, S., Schneider-Schaulies, J., Ohnimus, H., Jassoy, C., Schneider-Schaulies, S., Diamond, L., Logan, S. & ter Meulen, V. (1997 *b*). CD46 expression does not overcome the intracellular block of measles virus replication in transgenic rats. *Journal of Virology* **71**, 7969–7973.

Nomoto, A., Koike, S. & Aoki, J. (1994). Tissue tropism and species specificity of poliovirus infection. *Trends in Microbiology* **2**, 47–51.

Ogata, A., Czub, S., Ogata, S., Cosby, S. L., McQuaid, S., Budka, H., ter Meulen, V. & Schneider-Schaulies, J. (1997). Absence of measles virus receptor (CD46) in lesions of subacute sclerosing panencephalitis brains. *Acta Neuropathologica* **94**, 444–449.

Ohgimoto, S., Tabata, N., Suga, S., Nishio, M., Ohta, H., Tsurudome, M., Komada, H., Kawano, M., Watanabe, N. & Ito, Y. (1995). Molecular characterization of fusion regulatory protein-1 (FRP-1) that induces multinucleated giant cell formation of monocytes and HIV gp160-mediated cell fusion: FRP-1 and 4F2/CD98 are identical molecules. *Journal of Immunology* **135**, 3585–3592.

Ohta, H., Tsurudome, M., Matsumura, H., Koga, Y., Morikawa, S., Kawano, M., Kusugawa, S., Komada, H., Nishio, M. & Ito, Y. (1994). Molecular and biological characterization of fusion regulatory proteins (FRPs): anti-FRP mAb induced HIV-mediated cell fusion via an integrin system. *EMBO Journal* **13**, 2044–2055.

Okamoto, K., Tsurudome, M., Ohgimoto, S., Kawano, M., Nishio, M., Komada, H., Ito, M., Sakakura, Y. & Ito, Y. (1997). An anti-fusion regulatory protein-1 monoclonal antibody suppresses human parainfluenza virus type 2-induced cell fusion. *Journal of General Virology* **78**, 83–89.

Oldstone, M. B. A., Lewicki, H., Thomas, D., Tishon, A., Dales, S., Patterson, J., Manchester, M., Homann, D., Naniche, D. & Holz, A. (1999). Measles virus infection in a transgenic model: virus-induced immunosuppression and central nervous system disease. *Cell* **98**, 629–640.

Olsen, J., Cowell, G. M., Konigshofer, E., Danielsen, E. M., Moller, J., Laustsen, L., Hansen, O. C., Welinder, G. K., Engberg, J., Hunziker, W., Spiess, M., Sjöström, H. & Noren, O. (1988). Complete amino acid sequence of human intestinal aminopeptidase N as deduced from cloned cDNA. *FEBS Letters* **238**, 307–314.

Pileri, P., Uematsu, Y., Campagnoli, S., Galli, G., Falugi, F., Petracca, R., Weiner, A. J., Houghton, M., Rosa, D., Grandi, G. & Abrignani, S. (1998). Binding of hepatitis C virus to CD81. *Science* **282**, 938–941.

Putnak, J. R., Niranjan, K.-T. & Innis, B. L. (1997). A putative cellular receptor for dengue viruses. *Nature Medicine* **3**, 828–829.

Racaniello, V. R. (1996). Early events in poliovirus infection: virus–receptor interactions. *Proceedings of the National Academy of Sciences, USA* **93**, 11378–11381.

Radecke, F., Spielhofer, P., Schneider, H., Kaelin, K., Huber, M., Dötsch, C., Christiansen, G. & Billeter, M. A. (1995). Rescue of measles viruses from cloned DNA. *EMBO Journal* **14**, 5773–5784.

Raja, N. U., Vincent, M. J. & Jabbar, M. A. (1994). Vpu-mediated proteolysis of gp160/CD4 chimeric envelope glycoproteins in the endoplasmic reticulum: requirement of both the anchor and cytoplasmic domains of CD4. *Virology* **204**, 357–366.

Rall, G. F., Manchester, M., Daniels, L. R., Callahan, E. M., Belman, A. R. & Oldstone, M. B. A. (1997). A transgenic mouse model for measles virus infection of the brain. *Proceedings of the National Academy of Sciences, USA* **94**, 4659–4663.

Ren, R., Costantini, F., Gorgacz, E. J., Lee, J. J. & Racaniello, V. R. (1990). Transgenic mice expressing a human poliovirus receptor: a new model for poliomyelitis. *Cell* **63**, 353–362.

Rey, F. A., Heinz, F. X., Mandl, C., Kunz, C. & Harrison, S. C. (1995). The envelope glycoprotein from tick-borne encephalitis virus at 2 Å resolution. *Nature* **375**, 291–298.

Roelvink, P. W., Lizonova, A., Lee, J. G. M., Li, Y., Bergelson, J. M., Finberg, R. W., Brough, D. E., Kovesdi, I. & Wickham, T. J. (1998). The coxsackievirus–adenovirus receptor protein can function as a cellular attachment protein for adenovirus serotypes from subgroups A, C, D, E, and F. *Journal of Virology* **72**, 7909–7915.

Roelvink, P. W., Lee, G. M., Einfeld, D. A., Kovesdi, I. & Wickham, T. J. (1999). Identification of a conserved receptor-binding site on the fiber proteins of CAR-recognizing adenoviridae. *Science* **286**, 1568–1571.

Ruoslahti, E. & Reed, J. (1999). New way to activate caspases. *Nature* **397**, 479–480.

Samson, M., Libert, F., Doranz, B. J., Rucker, J., Liesnard, C., Farber, C. M., Saragosti, S., Lapoumeroulie, C., Cognaux, J., Forceille, C., Muyldermans, G., Verhofstede, C., Burtonboy, G., Georges, M., Imai, T., Rana, S., Yi, Y. J., Smyth, R. J., Collman, R. G., Doms, R. W., Vassart, G. & Parmentier, M. (1996). Resistance to HIV-1 infection in Caucasian individuals bearing mutant alleles of the CCR-5 chemokine receptor gene. *Nature* **382**, 722–725.

Schlender, J., Schnorr, J.-J., Spielhofer, P., Cathomen, T., Cattaneo, R., Billeter, M. A., ter Meulen, V. & Schneider-Schaulies, S. (1996). Interaction of measles virus glycoproteins with the surface of uninfected peripheral blood lymphocytes induces immunosuppression in vitro. *Proceedings of the National Academy of Sciences, USA* **93**, 13194–13199.

Schmid, E., Zurbriggen, A., Gassen, U., Rima, B. K., ter Meulen, V. & Schneider-Schaulies, J. (2000). Antibodies to CD9, a tetraspan transmembrane protein, inhibit canine distemper virus (CDV)-induced cell-cell fusion, but not virus-cell fusion. Submitted for publication.

Schneider-Schaulies, S. & ter Meulen, V. (1999). Measles virus induced immunosuppression. *Nova Acta Leopoldina* **307**, 185–197.

Schneider-Schaulies, J., Schnorr, J.-J., Brinckmann, U., Dunster, L. M., Baczko, K., Schneider-Schaulies, S. & ter Meulen, V. (1995*a*). Receptor usage and differential downregulation of CD46 by measles virus wild type and vaccine strains. *Proceedings of the National Academy of Sciences, USA* **92**, 3943–3947.

Schneider-Schaulies, J., Dunster, L. M., Kobune, F., Rima, B. K. & ter Meulen, V. (1995*b*). Differential downregulation of CD46 by measles virus strains. *Journal of Virology* **69**, 7257–7259.

Schneider-Schaulies, J., Schnorr, J.-J., Schlender, J., Dunster, L. M., Schneider-Schaulies, S. & ter Meulen, V. (1996). Receptor (CD46) modulation and complement-mediated lysis of uninfected cells after contact with measles virus-infected cells. *Journal of Virology* **70**, 255–263.

Schneider-Schaulies, J., Niewiesk, S., Schneider-Schaulies, S. & ter Meulen, V. (1999). Measles virus in the CNS: the role of viral and host factors for the establishment and maintenance of a persistent infection. *Journal of Neurovirology* **5**, 613–622.

Schnell, M. J., Johnson, J. E., Buonocore, L. & Rose, J. K. (1997). Construction of a novel virus that targets HIV-1-infected cells and controls HIV-1 infection. *Cell* **90**, 849–857.

Schnorr, J.-J., Dunster, L. M., Nanan, R., Schneider-Schaulies, J., Schneider-Schaulies, S. & ter Meulen, V. (1995). Measles virus-induced down-regulation of CD46 is associated with enhanced sensitivity to complement-mediated lysis of infected cells. *European Journal of Immunology* **25**, 976–984.

Shafren, D. R. (1998). Viral cell entry induced by cross-linked decay-accelerating factor. *Journal of Virology* **72**, 9407–9412.

Shafren, D. R., Bates, R. C., Agrez, M. V., Herd, R. L., Burne, G. F. & Barry, R. D. (1995). Coxsackieviruses B1, B3, and B5 use decay accelerating factor as a receptor for cell attachment. *Journal of Virology* **69**, 3873–3877.

Shieh, M. T., WuDunn, D., Montgomery, R. I., Esko, J. D. & Spear, P. G. (1992). Cell surface receptors for herpes simplex virus are heparan sulfate proteoglycans. *Journal of Cell Biology* **116**, 1273–1281.

Shiroki, K., Ishii, T., Aoki, T., Ota, Y., Yang, W. X., Komatsu, T., Ami, Y., Arita, M., Abe, S., Hashizume, S. & Nomoto, A. (1997). Host range phenotype induced in the internal ribosomal entry site of poliovirus RNA. *Journal of Virology* **71**, 1–8.

Shukla, D., Liu, J., Blaiklock, P., Shworak, N. W., Bai, X., Esko, J. D., Cohen, G. H., Eisenberg, R. J., Rosenberg, R. D. & Spear, P. G. (1999). A novel role for 3-O-sulfated heparan sulfate in herpes simplex virus 1 entry. *Cell* **99**, 13–22.

Siddell, S. G. (1995). The *Coronaviridae*: an introduction. In *The Coronaviridae*, pp. 1–10. Edited by S. G. Siddell. New York: Plenum Press.

Skehel, J. J., Steinhauer, D., Wharton, S. A., Bullough, P. A., Hughson, F. M., Watowich, S. J. & Wiley, D. C. (1994). Receptor binding and membrane fusion by influenza hemagglutinin. In *Cellular Receptors for Animal Viruses*, pp. 187–193. Edited by E. Wimmer. Cold Spring Harbour, NY: Cold Spring Harbour Laboratory Press.

Spear, P. G. (1993). Entry of alphaherpesviruses into cells. *Seminars in Virology* **4**, 167–180.

Spetz, A. L., Patterson, B. K., Lore, K., Andersson, J. & Holmgren, L. (1999). Functional gene transfer of HIV DNA by an HIV receptor-independent mechanism. *Journal of Immunology* **163**, 736–742.

Steinhauer, D. A., Sauter, N. K., Skehel, J. J. & Wiley, D. C. (1992). Receptor binding and cell entry by influenza viruses. *Seminars in Virology* **3**, 91–100.

Stephens, J. C., Reich, D. E., Goldstein, D. B., Shin, H. D., Smith, M. W., Carrington, M., Winkler, C., Huttley, G. A., Allikmets, R., Schriml, L., Gerrard, B., Malasky, M., Ramos, M. D., Morlot, S., Tzetis, M., Oddoux, C., di Giovine, F. S., Nasiolas, G., Chandler, D., Aseev, M., Hanson, M., Kalaydjieva, L., Glavac, L., Gasparini, P., Kanavakis, E., Claustres, M., Kambouris, M., Ostrer, H., Duff, G., Baranov, V., Sibul, H., Metspalu, A., Goldman, D., Martin, N., Duffy, D., Schmidtke, J., Estivil, X., O'Brien, S. J. & Dean, M. (1998). Dating the origin of the CCR5-delta 32 AIDS-resistance allele by coalescence of haplotypes. *American Journal of Human Genetics* **62**, 1507–1515.

Stevenson, S. C., Rollence, M., Marshall-Neef, J. & McLelland, A. (1997). Selective targeting of human cells by a chimeric adenovirus vector containing a modified fiber protein. *Journal of Virology* **71**, 4782–4790.

Stiasny, K., Allison, S. L., Marchler-Bauer, A., Kunz, C. & Heinz, F. (1996). Structural requirements for low-pH-induced rearrangements in the envelope glycoprotein of tick-borne encephalitis virus. *Journal of Virology* **70**, 8142–8147.

Sullivan, N., Sun, Y., Li, J., Hofmann, W. & Sodroski, J. (1995). Replicative function and neutralization sensitivity of envelope glycoproteins from primary and T-cell line-passaged human immunodeficiency virus type 1 isolates. *Journal of Virology* **69**, 4413–4420.

Summerford, C. & Samulski, R. J. (1998). Membrane-associated

heparan sulfate proteoglycan is a receptor for adeno-associated virus type 2 virions. *Journal of Virology* **72**, 1438–1445.

Tabata, N., Ido, M., Suga, S., Ohgimoto, S., Tsurudome, M., Kawano, M., Nishio, M., Watanabe, N., Okamoto, K., Komada, H., Sakurai, M. & Ito, Y. (1998). Protein tyrosine kinase activation provides an early and obligatory signal in anti-FRP-1/CD98/4F2 monoclonal antibody induced cell fusion mediated by HIV gp160. *Medical Microbiology and Immunology* **186**, 115–123.

Takahashi, K., Nakanishi, H., Miyahara, M., Mandai, K., Satoh, K., Satoh, A., Nishioka, H., Aoki, J., Nomoto, A., Mizoguchi, A. & Takai, Y. (1999). Nectin/PRR: an immunoglobulin-like cell adhesion molecule recruited to cadherin-based adherens junctions through interaction with afadin, a PDZ domain-containing protein. *Journal of Cell Biology* **145**, 539–549.

Tanaka, K., Xie, M. & Yanagi, Y. (1998). The hemagglutinin of recent measles virus isolates induces cell fusion in a marmoset cell line, but not in other CD46-positive human and monkey cell lines, when expressed together with the F protein. *Archives of Virology* **143**, 213–225.

Tanner, J., Weis, J., Fearon, D., Whang, Y. & Kieff, E. (1987). Epstein–Barr virus gp350/220 binding to B lymphocytes C3d receptor mediates adsorption, capping, and endocytosis. *Cell* **50**, 203–213.

Tedder, T. F., Goldmacher, V. S., Lambert, J. M. & Schlossman, S. F. (1986). Epstein–Barr virus binding induces internalization of the C3d receptors: a novel immunotoxin delivery system. *Journal of Immunology* **137**, 1387–1391.

Teng, M. N., Borrow, P., Oldstone, M. B. A. & de la Torre, J. C. (1996). A single amino acid change in the glycoprotein of lymphocytic choriomeningitis virus associated with the ability to cause growth hormone deficiency syndrome. *Journal of Virology* **70**, 8438–8443.

Thompson, P., Lu, J. & Kaplan, G. G. (1998). The cys-rich region of the hepatitis A virus cellular receptor 1 (HAVcr-1) is required for binding of hepatitis A virus and protective monoclonal antibody 190/4. *Journal of Virology* **72**, 3751–3761.

Tong, S., Li, J. & Wands, J. R. (1999). Carboxypeptidase D is an avian hepatitis B virus receptor. *Journal of Virology* **73**, 8696–8702.

Tresnan, D. B. & Holmes, K. V. (1998). Feline aminopeptidase N is a receptor for all group I coronaviruses. *Advances in Experimental Medicine and Biology* **440**, 69–75.

Triantafilou, M., Triantafilou, K., Wilson, K. M., Takada, Y., Fernandez, N. & Stanway, G. (1999). Involvement of β_2-microglobulin and integrin $\alpha_v\beta 3$ molecules in the coxsackievirus A9 infectious cycle. *Journal of General Virology* **80**, 2591–2600.

Tufaro, F. (1997). Virus entry: two receptors are better than one. *Trends in Microbiology* **5**, 257–258.

Urban, S., Breiner, K. M., Fehler, F., Klingmüller, U. & Schaller, H. (1998). Avian hepatitis B virus infection is initiated by the interaction of a distinct pre-S-subdomain with the cellular receptor gp180. *Journal of Virology* **72**, 8089–8097.

Urbanska, E. M., Chambers, B. J., Ljunggren, H. G., Norrby, E. & Kristensson, K. (1997). Spread of measles virus through axonal pathways into limbic structures in the brain of TAP −/− mice. *Journal of Medical Virology* **52**, 362–369.

Wadell, G. (1990). Adenoviruses. In *Principles and Practice of Clinical Virology*, 2nd edn, pp. 267–287. Edited by A. J. Zuckerman, J. E. Banatvala & J. R. Pattison. Chichester, UK: John Wiley & Sons.

Ward, T., Pipkin, P. A., Clarkson, N. A., Stone, D. M., Minor, P. D. & Almond, J. W. (1994). Decay-accelerating factor CD55 is identified as the receptor for echovirus 7 using CELICS, a rapid immuno-focal cloning method. *EMBO Journal* **13**, 5070–5074.

Warner, M. S., Geraghty, R. J., Martinez, W. M., Montgomery, R. I., Whitbeck, J. C., Xu, R., Eisenberg, R. J., Cohen, G. H. & Spear, P. G. (1998). A cell surface protein with herpesvirus entry activity (HveB) confers susceptibility to infection by mutants of herpes simplex virus type 1, herpes simplex virus type 2 and pseudorabies virus. *Virology* **246**, 179–189.

Weidmann, A., Maisner, A., Garten, W., Seufert, M., ter Meulen, V. & Schneider-Schaulies, S. (2000). Proteolytic cleavage of the fusion protein but not membrane fusion is required for measles virus-induced immunosuppression in vitro. *Journal of Virology* **74**, 1985–1993.

White, J. M. (1994). Fusion of influenza virus in endosomes: role of the hemagglutinin. In *Cellular Receptors for Animal Viruses*, pp. 281–321. Edited by E. Wimmer. Cold Spring Harbour, NY: Cold Spring Harbour Laboratory Press.

Wickham, T. J., Mathias, P., Cheresh, D. A. & Nemerow, G. R. (1993). Integrins $\alpha v\beta 3$ and $\alpha v\beta 5$ promote adenovirus internalization but not virus attachment. *Cell* **73**, 309–319.

Willett, B., Hosie, M., Shaw, A. & Neil, J. (1997). Inhibition of feline immunodeficiency virus infection by CD9 antibodies operates after viral entry and is independent of virus tropism. *Journal of General Virology* **78**, 611–618.

Williams, R. K., Jiang, G. S., Snyder, S. W., Frana, M. F. & Holmes, K. V. (1990). Purification of the 110-kilodalton glycoprotein receptor for mouse hepatitis virus (MHV)-A59 from mouse liver and identification of a non-functional, homologous protein in MHV-resistant SJL/J mice. *Journal of Virology* **64**, 3817–3823.

Williams, R. K., Jiang, G. S. & Holmes, K. V. (1991). Receptor for mouse hepatitis virus is a member of the carcinoembryonic antigen family of glycoproteins. *Proceedings of the National Academy of Sciences, USA* **88**, 5533–5536.

Wimmer, E., Harber, J. J., Bibb, J. A., Gromeier, M., Lu, H.-H. & Bernhardt, G. (1994). Poliovirus receptors. In *Cellular Receptors for Animal Viruses*, pp. 101–128. Edited by E. Wimmer. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press.

Wong, T. C., Yant, S., Harder, B. J., Korte-Safarty, J. & Hirano, A. (1997). The cytoplasmic domains of complement regulatory protein CD46 interact with multiple kinases in macrophages. *Journal of Leukocyte Biology* **62**, 892–900.

Yeager, C. L., Ashmun, R. A., Williams, R. K., Cardellichio, C. B., Shapiro, L. H., Look, A. T. & Holmes, K. V. (1992). Human aminopeptidase N is a receptor for human coronavirus 229E. *Nature* **357**, 420–422.

Yokomori, K. & Kai, M. L. (1992). Mouse hepatitis virus utilizes two carcinoembryonic antigens as alternative receptors. *Journal of Virology* **66**, 6194–6199.

Yoshiyama, H., Imai, S., Shimizu, N. & Takada, K. (1997). Epstein–Barr virus infection of human gastric carcinoma cells: implication of the existence of a new virus receptor different from CD21. *Journal of Virology* **71**, 5688–5691.

Zelus, B. D., Wessner, D. R., Williams, R. K., Pensiero, M. N., Phibbs, F. T., DeSouza, M., Dveksler, G. S. & Holmes, K. V. (1998). Purified, soluble recombinant mouse hepatitis virus receptor, Bgp1b, and Bgp2 murine coronavirus receptors differ in mouse hepatitis virus binding and neutralization activities. *Journal of Virology* **72**, 7237–7244.