Retroviruses

Retroviruses belong to a group of unusual viruses. They are coated with a phospholipid membrane, have oncogenic potential, cause unfortunate, often fatal diseases, and can reprogram cellular DNA . In the nucleocapsid, two identical ssRNA (+) molecules and the enzyme carry a reverse transcriptase that transcribes the retrovirus genome first into the ssDNA (-). The resulting RNA-DNA hybrid is digested with RNase H and the remaining RNA fragments serve as primersfor the synthesis of the second strand of DNA. The resulting double-stranded cDNA is integrated into the cellular DNA in the form of a provirus by viral integrase upon entry into the nucleus. Provirus has long terminal repeats at both ends, which are strong promoters and also contain a polyadenylation signal. Integration of the provirus into the host genome not only ensures the expression of viral mRNAs , but also affects the expression of surrounding genes, which can cause cancer growth.

Classification

Retroviruses are classified into three subfamilies: *Oncovirinae* , *Lentivirinae* and *Spumavirinae* or into two subfamilies: *Spumaretrovirinae* and *Orthoretrovirinae* according to morphological differences, gene expression and viral gene processing.

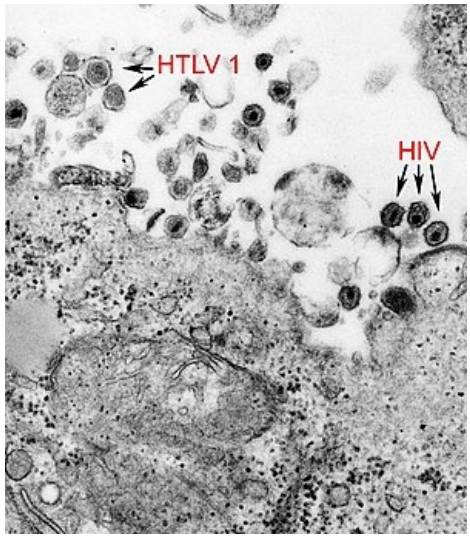
Orthoretrovirinae *includes* all oncogenic retroviruses and, based on their morphological features and genome complexity, is further classified into seven groups:

- simple - *alpha-* , *beta-* and *gammaretroviruses* ;
- complex - *delta-* , *epsilon-* , *lentiviruses* and *spumaviruses* .

The main difference between them is that complex retroviruses also have genes in their genome for non-structural proteins that facilitate virus replication or neutralize non-specific and specific immunity during infection .

HTLV-1

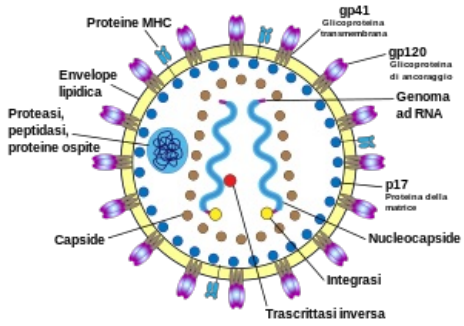
One of the complex retroviruses is HTLV-1 , which is a *deltaretrovirus* . In addition to the usual structural genes (*gag* , *pol* and *env*), it has several open reading frames in its genome in the pX region at the 3 'end. Regulatory proteins (eg Tax - a strong enhancer of viral gene expression and malignant transformation) and 3 additional proteins (p12, p13 and p30 - important for viral infectivity) are encoded in this area . Malignant transformation is caused by continuous stimulation of the proliferation of infected cells and cell immortality *in vitro*



HIV

The most complex retrovirus is HIV , whose genome has nine genes . It belongs to the *lentiviruses* . Non-structural gene products, regulatory proteins , are involved in transactivating viral mRNA expression, regulate viral pre-mRNA splicing, and suppress the immune response. The structural genes encode the capsid polyprotein Gag, the reverse transcriptase Pol and the envelope glycoprotein Env. Env (respectively its surface subunit gp120) recognizes the cellular receptor CD4 and the co-receptor CCR5, after interacting with them the conformation of Env changes, the fusion of the viral and cell membrane and the entry of the virion into the cytoplasm of the cell.

HIV, HTLV-1 and The Blood Brain Barrier



HIV (*lentivirinae*) is the cause of AIDS and HTLV-1 (*onkovirinae*) is the cause of ATL (adult T-cell leukemia), which are very serious and complex diseases. At the same time, we must point out that various neuropathological changes also take place at the level of the blood-brain barrier .

HAM/TSP

These include HAM / TSP (HTLV-1 associated myelopathy / tropical spastic paraparesis). This is rare (occurring in less than 3% of people infected with HTLV-1 virus), a slowly progressing neurological disease characterized by immunoglobulin and fibrinogen deposits in the brain parenchyma and the passage of infected lymphocytes across the blood-brain barrier. In one study with human brain endothelial cells, it was demonstrated that infected lymphocytes are able to alter the structure of tight junctions , increase paracellular permeability and transcellular migration. This is achieved by the secretion of

IL-1alpha and TNF-alpha. In addition, cerebral endothelial cells can be infectedHTLV-1 virus, as confirmed by spinal cord autopsy from HAM / TSP patients, is another mechanism of changes in the blood-brain barrier (such an infection is proliferative in vitro) and the entry of viruses into the CNS .

HAD and HIVE Mechanisms

Neuropathological changes in the blood-brain barrier are also present during HIV infection. Although infection of endothelial cells with HIV is a reason for further research, it is thought that such infections may have a detrimental effect on the function of this barrier by allowing these infected cells to secrete metalloproteases, cytokines and the viral protein Tat , or to undergo apoptosis .

The viral protein Tat , which is secreted by infected cells (not just endothelial), is able to cross the cell membrane and is detectable in the serum and cerebrospinal fluid of infected HIV patients. Its side effect is mediated by activation of extracellular signal-regulating kinase ½ (ERK1 / 2 pathway). The resulting increased oxidative stress can cause an increase in intracellular calcium concentration , which causes mitochondrial dysfunction and subsequent endothelial cell apoptosis. Endothelial cell apoptosis has been observed in some AIDS patients . In addition to being a tool for the adsorption of virions to cellular receptors, the gp120 glycoprotein also induces the secretion of*metalloproteases-2* , oxidative stress and degradation of *ZO-1* and *occludin* together with changes in *claudin* expression . In this way, the blood-brain barrier function is impaired and infiltration by infected monocytes is increased.

During the asymptomatic phase of HIV infection, chronic activation of the immune system is present, accompanied by dysregulation of cytokine secretion. At this stage , HIV can be detected in the cerebrospinal fluid. It gets here by migrating activated and infected CD4 + T-cells , monocytes or dendritic cells from the periphery. Once in the CNS, virus replication begins, accompanied by massive secretion of cytokines and chemokines in the CNS. Cerebral endothelial cell function is severely impaired due to this chronic activation, and this results in increased expression of cell adhesion markers such as ICAM-1 (intercellular adhesion molecule-1), the secretion of metalloproteases that induce lamina basalis thinning.. All this facilitates the extravasation of mononuclear cells into the CNS.

The neurological symptoms associated with HIV infection are HAD (HIV-associated dementia) and HIVE (HIV-encephalitis). These symptoms can occur without the presence of opportunistic infections. Cognitive and motor disorders are typical for them: limb muscle weakness, memory disorders , depression and dementia .

Links

Related Articles

- AIDS
- HIV
- Diagnostika AIDS

External Links

- Retrovirus (česká wikipedie) (https://cs.wikipedia.org/wiki/Retroviry%7C)
- Retrovirus (anglická wikipedie) (https://en.wikipedia.org/wiki/Retrovirus%7C)

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