**Viral mediated Gene Transfer**

Particular viruses have been selected as gene delivery vehicles because of their capacities to carry foreign genes and their ability to efficiently deliver these genes associated with efficient gene expression.

**Principle**

In general, the achieved transfection efficiencies in primary cells and cell lines are high. The first step in the infection cycle of a virus is the interaction between the virus and a cellular receptor on the surface of a target cell, resulting in the fusion of the viral and the cellular membrane. Cells which are not carrying such a receptor cannot be infected by the virus.

Limitations of viral gene transfer are:

* Time consuming and laborious production of vectors
* Elevated laboratory costs due to higher biosafety level requirements
* Limitation of insert size (~10 kb for most viral vectors versus ~100 kb for non-viral vectors)
* Variability in infection potencies of the generated virus particle preparations
* Possible immunogenic reaction in animal or clinical trials.

Well-known examples for viral gene transfer vectors are recombinant adenoviruses, retroviruses, adeno-associated viruses, herpes simplex viruses and vaccinia viruses.

**Adenoviruses** have a broad cell tropism and can infect both dividing and non-dividing cells. Exceptions are some lymphoid cells, which are more resistant to adenoviral infection than other cell types.

* The packaging capacity of adenoviral vectors is 7 to 8 kb. Unlike retroviruses, adenoviruses allow production of 1010 to 1011 viral particles/ml which can be concentrated up to 1013 viral particles/ml.
* One disadvantage of adenoviral vectors is their episomal status in the host cell, allowing only transient expression of the transgene. This also means that adenoviruses do not interfere with the host genome.
* Expression of adenoviral proteins like E2 provokes inflammatory reactions and toxicity that limit the repeated application of adenoviral vectors for gene therapy.

**Retroviruses** make excellent gene therapy vectors because they have the ability to integrate their genome into a host cell genome, thus enabling stable expression of the transgene.

* Most retroviruses are limited by the requirement of replicating cells for infection. An exception are the lentiviruses (subgroup of retroviruses), which have the ability to infect and integrate into non-dividing cells. Based on this feature, the use of lentiviral- based vectors could be of great value for gene delivery to tissues of non-dividing, terminally differentiated cell populations, such as neuronal tissue, hematopoietic cells, myofibers etc.
* Like adenoviruses, retroviruses can carry foreign genes of around 8 kb.
* Among the disadvantages are the instability of some retroviral vectors and possible insertional mutagenesis by random integration into the host DNA.

**Adeno-associated** viruses need helper viruses like adenovirus or herpes virus for lytic infection. This causes difficulties in obtaining high quality viral stocks free of helper viruses.

* The adeno-associated viruses have only limited capacity for insertion of foreign genes ranging up to 4.9 kb.
* Wildtype viruses have the ability to integrate into a specific region of the human chromosome, thus avoiding insertional mutagenesis.
* Another advantage is the low immunogenicity of adeno-associated viruses, which is important for the application in human gene therapy.
* It has been shown that recombinant adeno-associated vectors are suitable for in vitro and in vivo gene transfer into e.g., muscle, brain, hematopoietic cells, neurons and liver cells.

Besides retroviruses, adenoviruses and adeno-associated viruses, herpes simplex viruses and vaccinia viruses are frequently used for viral gene transfer. They have the ability to carry large inserts up to 50 kb. Herpes simplex viruses have been used for gene transfer into neurons, brain tumors, various tumor cells and B cells. One disadvantage of herpes simplex viruses is that they may become latent in neural cells and that there is so far little information of the fate or stability of the vector. On the other hand, latency may be an advantage for stable gene expression in chronic diseases.

**A Comparison of Different Viral Systems**

