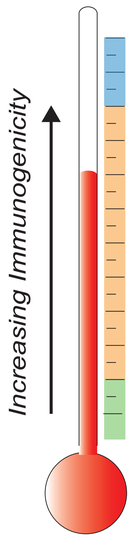
Beginner's Guide to Viral Vectors

Immunogenicity

How will cells react to my virus?



Highly immunogenic adenoviruses can be beneficial in some instances, for example, as vaccines or to deliver cancer therapeutics by acting as an oncolytic virus.

Retroviruses are the most popular virus for gene transfer in clinical trials because of their high/ stable expression and mild immunogenicity.

Mildly immunogenic viruses like adeno associated vrius (AAV), lentivirus, and retrovirus are popular for *in vivo* research.

Packaging Capacity

How much genomic material can be delivered?

Recombinant viruses used for research have been derived from wild-type viruses and modified for safety and efficiency. These modifications enable the virus to direct expression of specific transgenes, whose sequences are packaged within the virus. Due to physical restrictions based on the size of the virion, the length of the transgenes delivered by viral vectors is limited by the packaging capacities below.

Adenovirus

37 kb **Goncalves et al., 2001*

Retrovirus/Lentivirus

7 - 9 kb (but up to 19 kb with dramatic titer decrease) **Kumar et al., 2001*

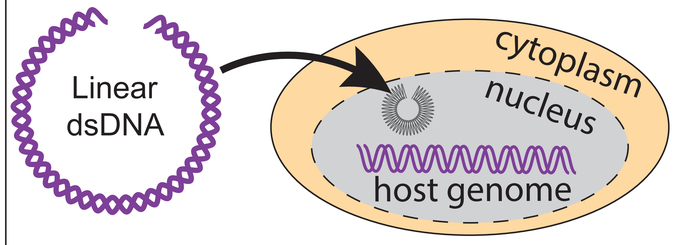
Adeno-associated Virus

4 - 5 kb

Genome Composition

What is the structure of the viral genome and where does it integrate in the host cell?

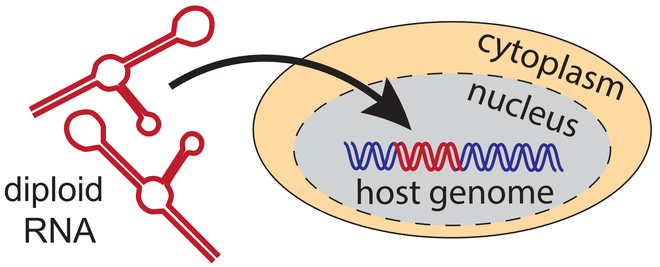
Adenovirus



- Genome is linear, double-stranded DNA incorporated with proteins; structure not fully known.
- Can transduce both dividing and non-dividing cells.
- Remains Episomal in host and is lost (not replicated) upon cell division.

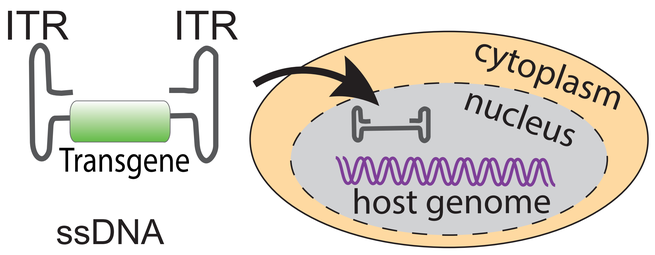
**Goncalves et al., 2001*

Retrovirus/Lentivirus



- Genomes are single-stranded RNA that adopt loop and stem structures.
- Viral genome is reverse transcribed and then integrates randomly into the host genome.
- Random integration has the potential to cause insertional mutagenesis.
- Retrovirus depends on the mitotic breakdown of the nuclear envelope for nuclear entry and transduction.
- Integrated viral sequences are replicated during cell division, leading to long term transgene expression.
- Lentivirus can transduce dividing and non-dividing cells.

Adeno Associated Virus



- Single-stranded DNA genome; exhibits a hairpin structure at the ITRs.
- Recombinant AAV typically remains episomal and is lost (not replicated) upon cell division.
- Wild-type AAV integrates into the host genome in approximately 0.1% of cases and at a specific site on chromosome 19 termed the AAVS1 site.
- Integration is dependent on the rep protein so integration of recombinant AAV (which lack rep) is rare.
- Transduction does not require cell division.

**Goncalves et al., 2001*

Need More Info on Virus?
addgene.org/viral-vectors

addgene
The nonprofit plasmid repository