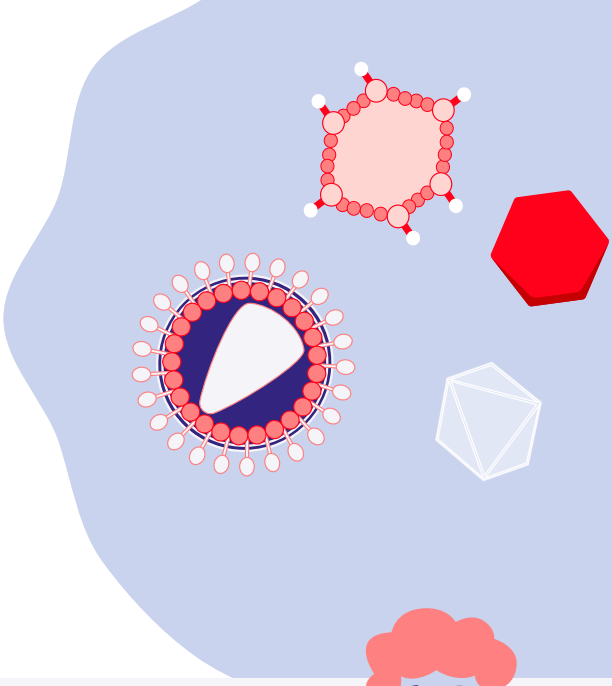
Viral Vector Overview



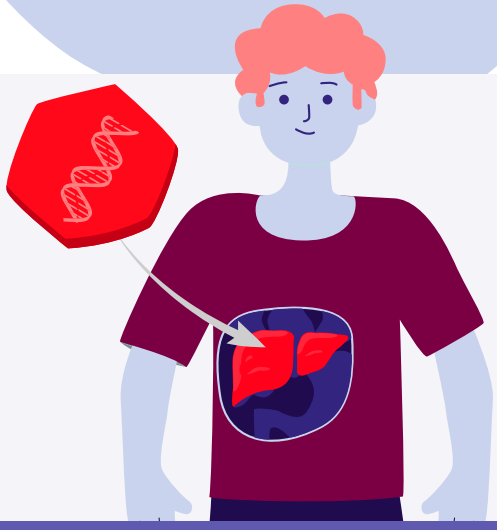
Why Viruses?

A vector is a vehicle used to deliver therapeutic genetic material - DNA or RNA - into a cell. For gene therapy, there are four main types of vectors, all derived from viruses because a virus is good at getting into cells. But the viral genes are removed, so only the therapeutic genes are delivered. Researchers carefully choose which viral vector to use to treat a disease based on:

- How well researchers understand the virus
- How well the virus can target certain cells
- How safe it is to use

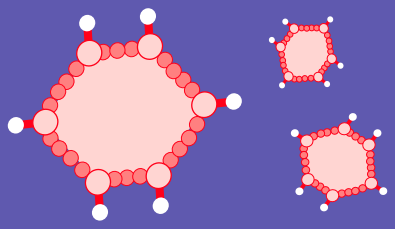
Adeno-Associated Viral (AAV) Vectors

- Are able to deliver only small DNA packages, or genes, to cells
- Are non-integrating, or don't insert themselves into cells' genome
- Are typically used to target non-dividing cells, such as liver or nerve cells
- Are most effective for *in vivo* treatments when vectors are injected directly into the body
- Can be limited by innate immunity since many people are exposed to AAVs through natural infections. The immune cells may destroy the vector before it can deliver the therapy
- Can be limited to a single dose since antibodies may develop



Adenoviral Vectors

- Can deliver packages up to 8x larger than AAVs
- Are similar to AAVs in that they are non-integrating into the cells' genome and target non-dividing cells
- Can cause strong immune responses resulting in potentially harmful inflammation throughout the body, that decreases treatment effectiveness. Scientists are working to improve this vector type to have a milder response



Lentiviral + Retroviral Vectors

- Can deliver larger genetic packages of RNA, which is converted into DNA. During this process, the vectors integrate into the genome of the target cell
- Are typically used to target dividing cells, like T cells, which are immune cells, and stem cells. The new genetic material is copied into all the new cells beyond the original cell
- Are most effective for *ex vivo* treatments when the person's cells are removed from the body, modified by vectors delivering working genes, and then returned to the body to improve function