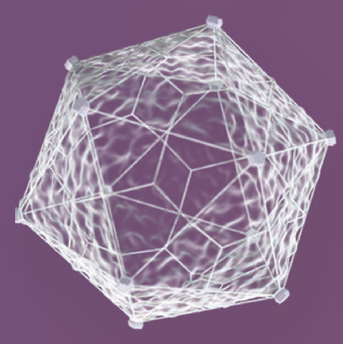
Anatomy of an AAV Vector

Transgene

The transgene encodes the protein to be produced, e.g., factor VIII or IX

Expression Cassette

The transgene with elements to allow it to produce protein (e.g., FVIII or FIX), such as a liver-selective promoter, leader sequence, and poly-A signal, and inverted terminal repeats

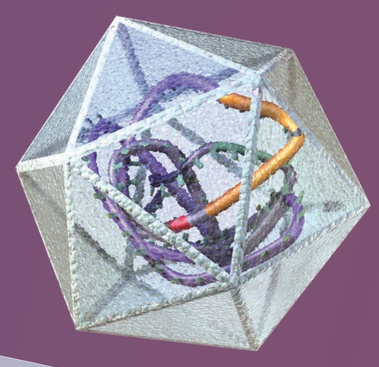


Capsid

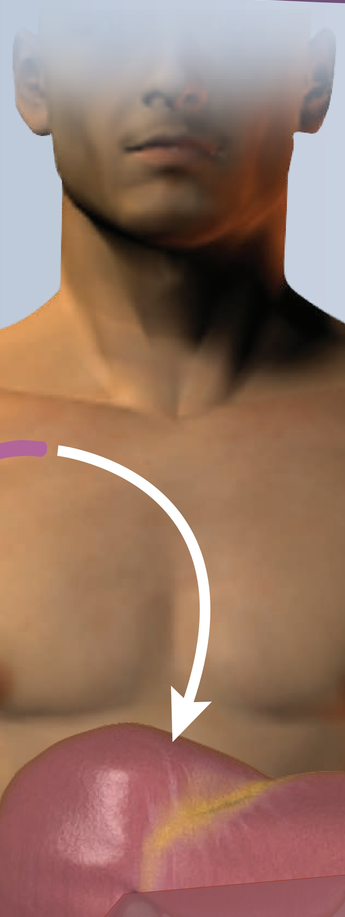
Viral gene depleted AAV shell

Vector

Capsid containing the expression cassette

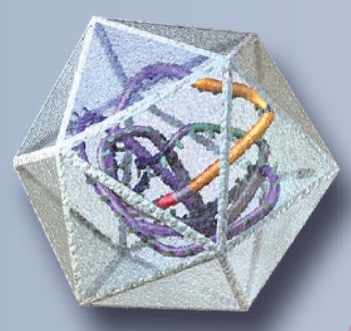


Researching: Mechanism of Action



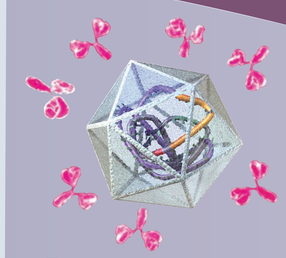
1

Vector is infused into the patient via a peripheral vein



2

Vector binds to a target cell (e.g., hepatocyte) and enters the cell

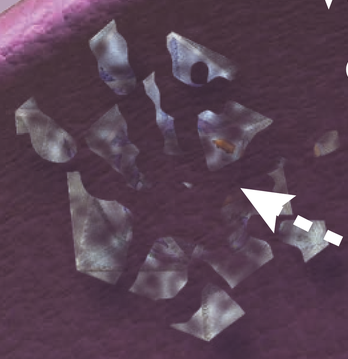


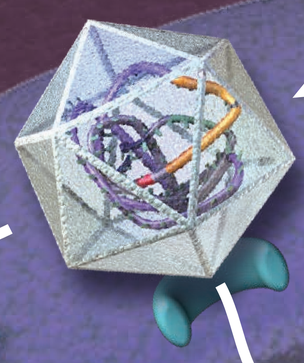
Pre-existing antibodies against AAV may prevent the vector from entering the hepatocyte

Scan QR code to learn more

3

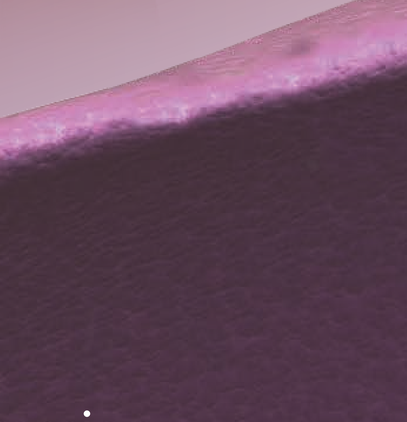
Vector deposits expression cassette into the nucleus and then the capsid degrades





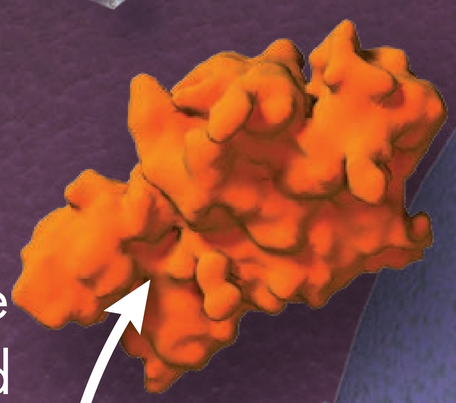
4

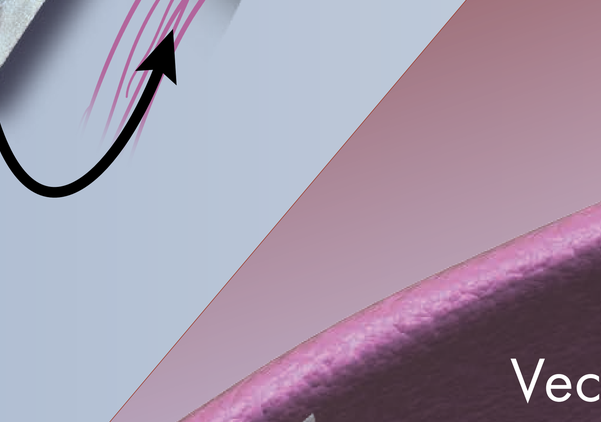
The expression cassette is designed to exist as a circular piece of DNA, called an episome



5

From the episomal expression cassette, the transgene is transcribed and translated to produce protein





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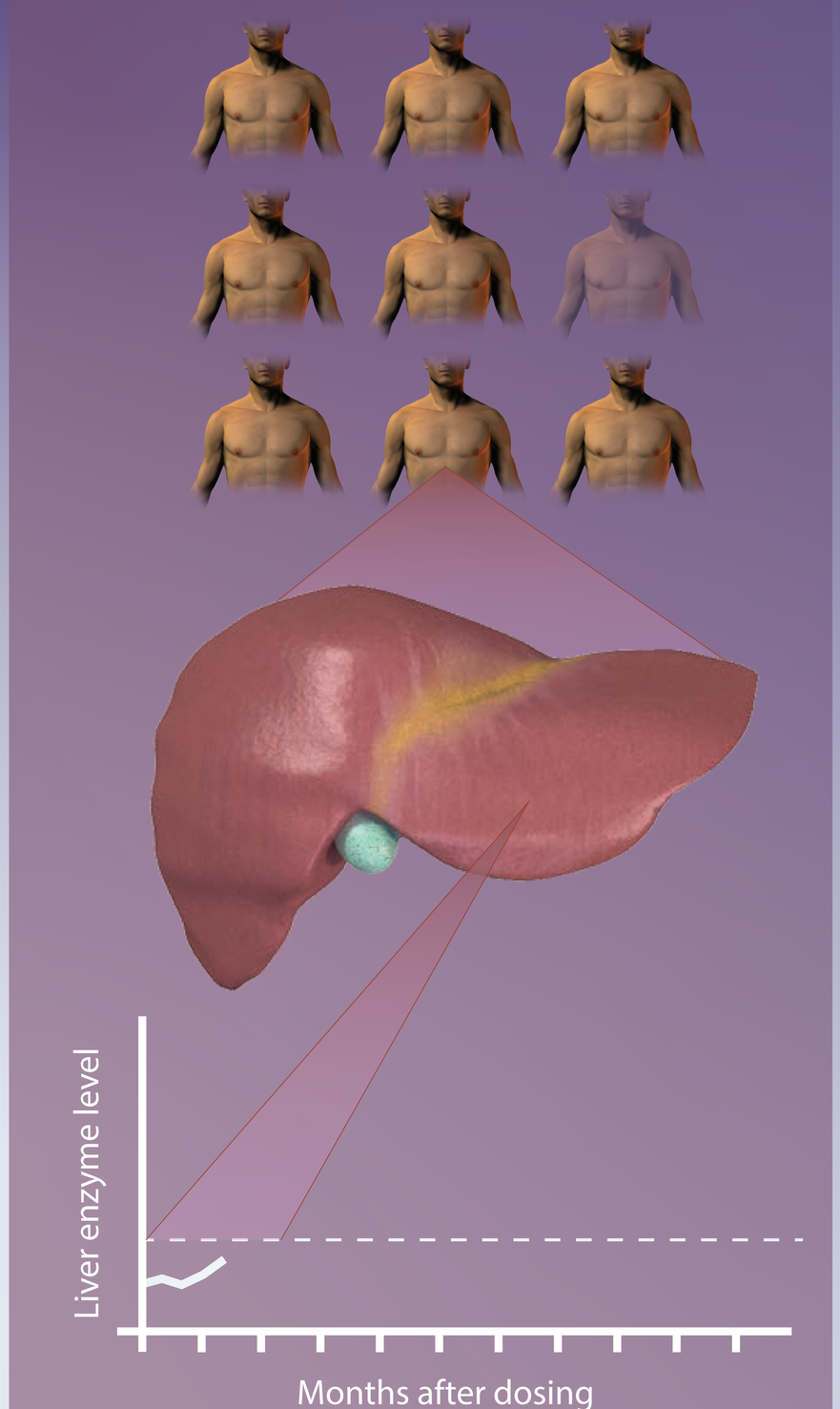
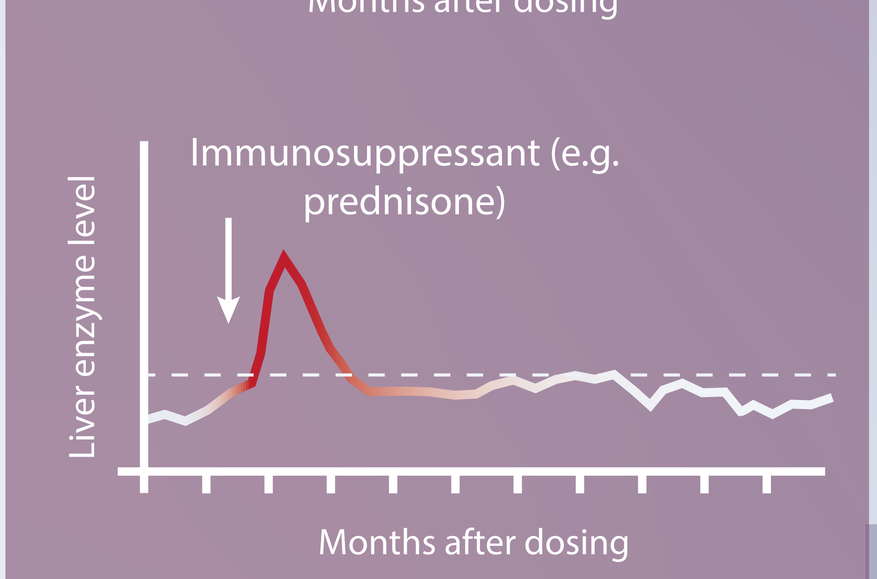
Goal: Optimizing Transgene Expression

Liver-Targeted AAV Gene Therapy Research for Hemophilia A and B





Patient Selection

As the target organ to produce therapeutic protein, liver health is considered in patient selection. Specific liver-related criteria used in hemophilia gene therapy trials include:

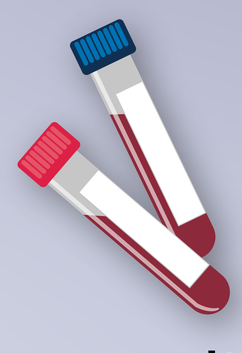
- ✓ No significant liver dysfunction
- ✓ No significant liver fibrosis or cirrhosis
- ✓ No active viral hepatitis B or C, chronic hepatitis B

Post Gene Transfer

Clinical trials for hemophilia have followed a similar protocol for monitoring and management of the liver post-infusion:

Scan the QR code to test your knowledge of AAV gene therapy research!

Monitor liver enzymes



Typically weekly immediately following and gradually less frequently through the first year following gene transfer.

Manage liver enzyme elevations with immunosuppressants

Use immunosuppressants in patients who experience transient transaminitis.

Transient liver enzyme elevation

and/or immunosuppressant use has been observed with all investigational liver-targeted AAV gene therapies being researched for hemophilia A or B

Liver-targeted
AAV gene therapy research for hemophilia A or B

30 +	300 +	Up to 8
Clinical trials registered	Trial participants enrolled	Years of follow-up clinical data published

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