Voyager® THERAPEUTICS

WORKING TO DEVELOP LIFE-CHANGING AAV GENE THERAPY TREATMENTS FOR PEOPLE WITH SEVERE NEUROLOGICAL DISEASES

Path to developing gene therapy treatments for severe neurological diseases

IDENTIFY THERAPEUTIC GENE AND ANATOMICAL TARGET

ENGINEER TARGET-SPECIFIC VECTORS FOR GENE THERAPY

IDENTIFY AND SUPPORT ADVANCEMENT OF STATE-OF-THE-ART CNS DELIVERY

Identification of the therapeutic gene and anatomical target along with route of administration are required for gene therapy vector development

THERAPEUTIC GENE

The therapeutic gene is identified based on understanding of the disease biology.

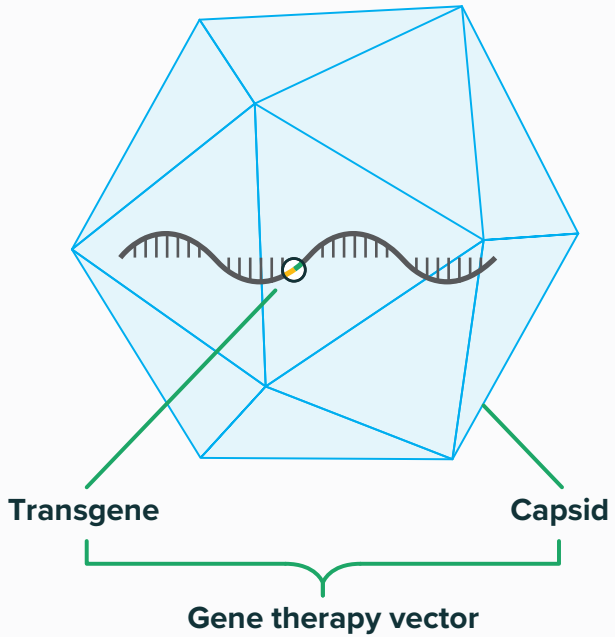
THERAPEUTIC ACTION

Therapeutic action is designed to achieve replacement, knockdown, or supplementation of the therapeutic gene based on molecular defects expected to impact disease pathology.

ANATOMICAL TARGET

The anatomical target likely to have the greatest impact on disease pathology is identified and informs administration.

Gene therapy vectors include a combination of capsid and transgene that have been selected or engineered based on the therapeutic gene and action, anatomical target, and route of administration



THE CAPSID

The non-pathogenic outer shell of adeno-associated virus (AAV) is used to deliver the transgene (ie, therapeutic payload) to target cells. Capsids can be engineered to exhibit desired properties such as tropism (cell targeting and de-targeting) and the ability to cross the blood-brain barrier (BBB).

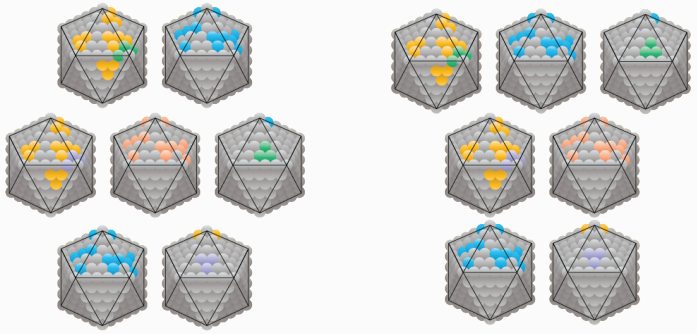
THE TRANSGENE

Purpose-engineered therapeutic gene and gene-regulatory elements that control expression (eg, promoter sequence) are flanked by inverted terminal repeats (ITR) and packaged inside the capsid.

AAV capsids are particularly well-suited to deliver transgenes for the treatment of neurological diseases

Natural AAV Capsids

Engineered AAV Capsids



NATURAL AAV CAPSIDS

Several natural serotypes of AAV have been isolated from human and non-human tissue that display a variety of attributes well-suited for CNS gene therapy development including selective tissue targeting (tropism), ability to cross the BBB, and non-integrating gene transfer.

ENGINEERED AAV CAPSIDS

Comprehensive understanding of capsid biology can be used to engineer novel AAV capsids with desired attributes for specific application in CNS gene therapy development.

AAV CAPSID USE IN THE CLINICAL SETTING

AAV capsids are utilized in current FDA/EMA-approved CNS gene therapies and have been tested in more than 150 clinical trials.

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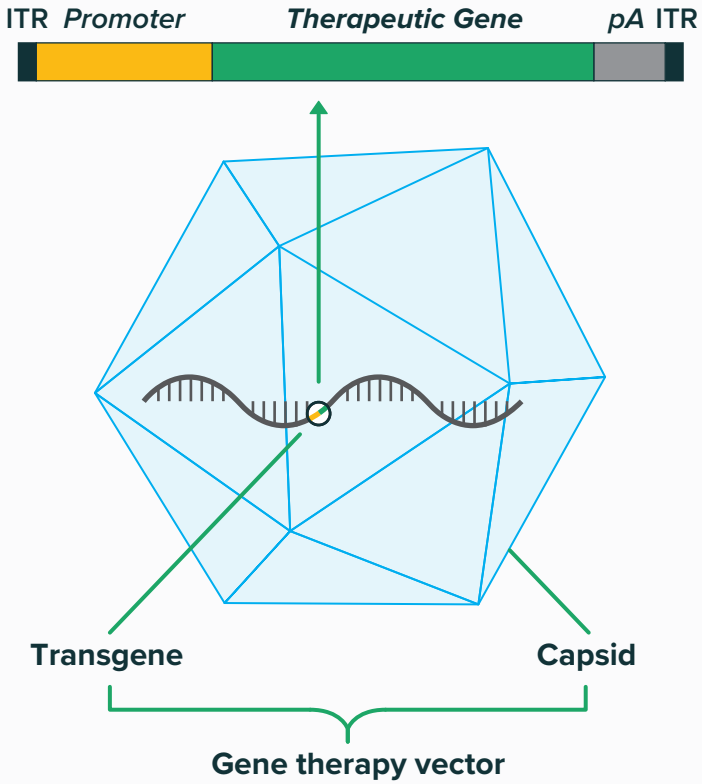
Transgenes include a purpose-engineered therapeutic gene, along with regulatory elements to control therapeutic gene expression and signature inverted terminal repeats on each end



THERAPEUTIC GENE

Purpose-engineered gene designed to achieve the therapeutic action.

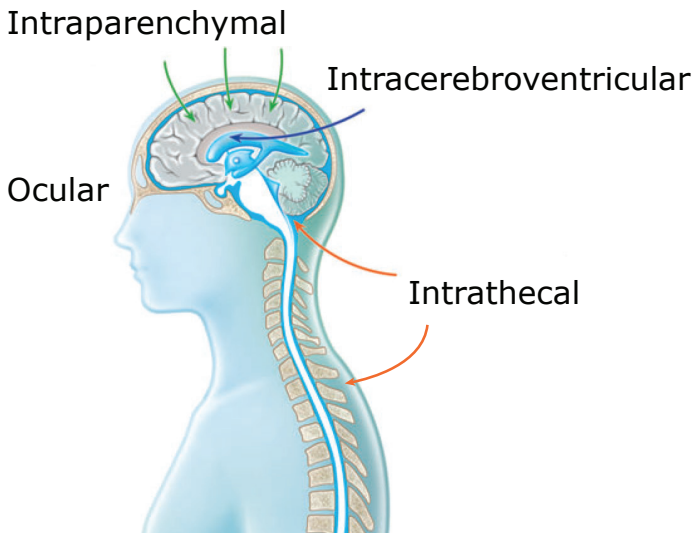
REGULATORY ELEMENTS

Parts of the transgene that regulate expression of the therapeutic gene. Examples include promoters that drive gene expression within target cell populations.

INVERTED TERMINAL REPEATS

ITRs are DNA sequences that flank the two ends of the transgene and ensure its packaging within the AAV capsid. Within the nucleus, ITRs enable formation of circular transgene episomes that persist alongside the host chromosome and utilize cell machinery to express the therapeutic gene.

State-of-the-art delivery enables patient-specific, precision administration of CNS gene therapy



IDENTIFY ADMINISTRATION NEEDS

The combination of route of administration, delivery parameters, and formulation is selected with the goal of achieving safe and effective gene therapy within disease-specific CNS targets.

STATE-OF-THE-ART CNS DELIVERY

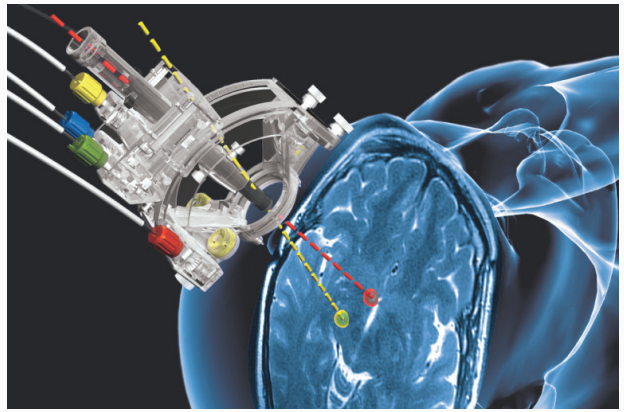
Therapeutic target and capsid properties require different approaches for vector delivery including focal (eg, intraparenchymal infusion coupled with real-time MRI) and broad (eg, CSF injection, intravenous) CNS delivery.

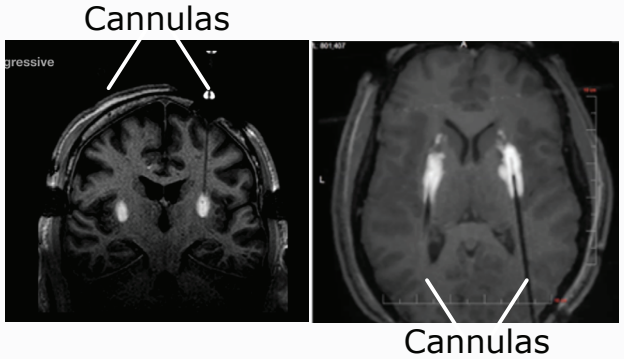
IDENTIFY THERAPEUTIC GENE AND ANATOMICAL TARGET

ENGINEER TARGET-SPECIFIC VECTORS FOR GENE THERAPY

IDENTIFY AND SUPPORT ADVANCEMENT OF STATE-OF-THE-ART CNS DELIVERY

Stereotactic-guided convection-enhanced delivery (CED) with MRI-assisted intraparenchymal infusion enables patient-specific, precision delivery to CNS targets





STEREOTACTIC-GUIDED INTRAPARENCHYMAL INFUSION

An established surgical intervention that uses a three-dimensional coordinate system to locate targets within the brain. Shown to be a well-tolerated and effective approach for precise delivery of gene therapy to target areas of the brain.

CONVECTION-ENHANCED DELIVERY

CED provides measurable, consistent, and predictable infusion rates along with distribution of high macromolecule concentrations over large parenchymal volumes.

MAGNETIC RESONANCE IMAGING

Preoperative use permits mapping of patient-specific cannula trajectories. Intraoperative use permits real-time visualization of cannula tip position and gene therapy vector distribution for precise delivery of infusion volumes to enable effective target coverage with minimal off-target delivery.

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