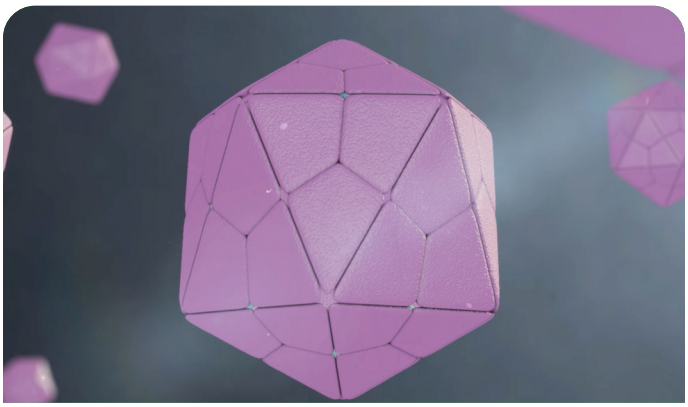
CHILDREN'S MEDICAL RESEARCH INSTITUTE

Jeans for Genes®

Gene Therapy
AAV Vector Development Program

Introduction

Gene therapy is a rapidly growing area in the biotechnology landscape with AAV vectors being some of the most important tools in the space. With the recent FDA approval of AAV2-based Luxturna (Spark Therapeutics), the pharmaceutical industry is beginning to realize the transformative potential of gene therapies. However, to treat and potentially cure the wide array of genetic diseases that are candidates for gene therapy, a transition must be made to next generation AAV vectors. To this end, CMRI's comprehensive Vector Development Program enables identification of novel AAV vectors with a variety of enhanced characteristics and increased commercial potential.



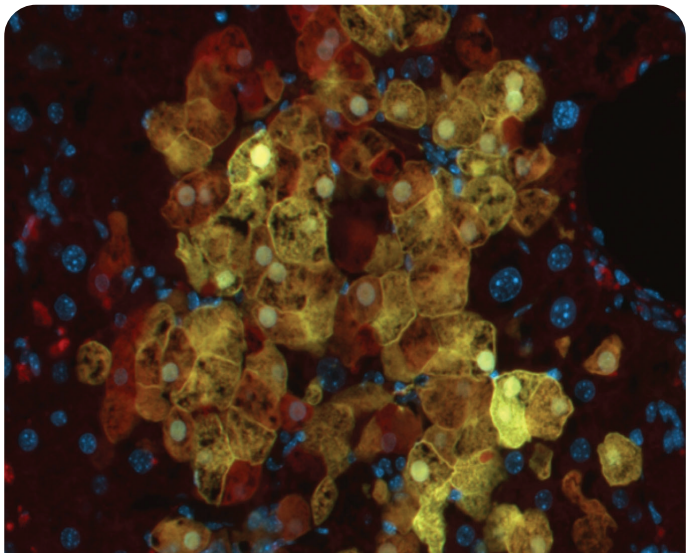
Problem

Early generation AAVs, such as the AAV2 used in Luxturna and most AAVs currently in clinical trials, were identified in nature. They have been adopted as gene therapy tools because they have a good safety record, the ability to transduce both dividing and non-dividing cells, and some degree of tissue specificity. However, these naturally occurring viruses have not been optimized for clinical effectiveness or manufacturing efficiency.

For maximal clinical effectiveness, vectors should be optimized to achieve functional transduction of target tissues with high efficiency and high specificity. Low efficiency transduction and low tissue specificity can lead to decreased effectiveness, increased probability of toxicity and immunological reaction, and increased doses of AAV per patient. With higher doses, or with inefficient manufacturing, scalability and costs of vector production become problematic. These two inter-related issues, vector functionality and manufacturing efficiency, must be optimized together to enable commercial viability and success.

Solution

From the start of the vector design process, our AAV Vector Development Program employs proprietary technology and unique expertise to concurrently optimize both vector functionality and manufacturability. Our capabilities allow identification of the most functional clinical candidates while simultaneously de-risking clinical development by addressing vector manufacturability and other CMC components. This integrated approach seeks to "begin with the end in mind" and results in vectors that are optimised for clinical and commercial success.



Transduction of primary human hepatocytes with new generation AAV capsids

Competitive Advantages

We have a diverse array of capabilities that enable production of next generation AAV vectors.

Vector Functionality:

- Unique know-how around capsid discovery, engineering, development, optimisation and testing
- Expertise with and access to primary human tissue and clinically predictive in vitro and in vivo model systems
- Patent families covering use of novel, diverse AAV inputs and AAV library platforms

Together, our capabilities around vector functionality constitute an established and tested pipeline allowing for generation and selection of novel AAV variants with superior functional profiles in human tissues.

Market Size

Globally there are over 300 active AAV programs between 114 AAV companies

The global market for gene therapy is projected to exceed US$11 billion by 2025

The vector manufacturing market is expected to exceed US$800m in 2023, representing a 5 year CAGR of 20%

Vector Manufacturability:

- Improved manufacturing protocols to maximise particle output per packaging cell
- Highly modular and flexible selection systems, reagents and protocols
- Evaluation based on diverse measures, including functionality, physico-chemical stability and yield

Our proprietary technology, expertise and the robust systems we have established allow us to optimize individual components of the manufacturing process while simultaneously optimizing vector functionality

Clinical-grade Manufacturing:

- In partnership with the Sydney Children's Hospital Network (SCHN), a small scale AAV GMP manufacturing facility is planned and will be funded with a grant from the NSW government
- Once established, the facility will enable production of material suitable for clinical trials and will operate as a service facility providing support to clients from bench to bedside

Overall, we have unique advantages in the gene therapy space as a result of our:

- Integrated approach to optimizing both vector functionality and manufacturability
- Broad expertise around capsid development and optimisation
- Multiple patent families protecting highly relevant proprietary technology

Please contact

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The Sydney children's Hospitals Network
care, advocacy, research, education

References

Global market 11 billion by 2025: https://apply-for-innovation-funding.service.gov.uk/competition/76/overview#supporting-information
CAGR of 19.5% 2018-2023: https://www.mordorintelligence.com/industry-reports/viral-vectors-and-plasmid-dna-manufacturing-market
CAGR of 20% 2018-2023: https://www.marketsandmarkets.com/PressReleases/viral-vector-manufacturing.asp