Plasmid engineering to improve AAV productivity and packaging efficiency

Innovate together with Lonza in Your Lab®

Lonza
Cell & Gene

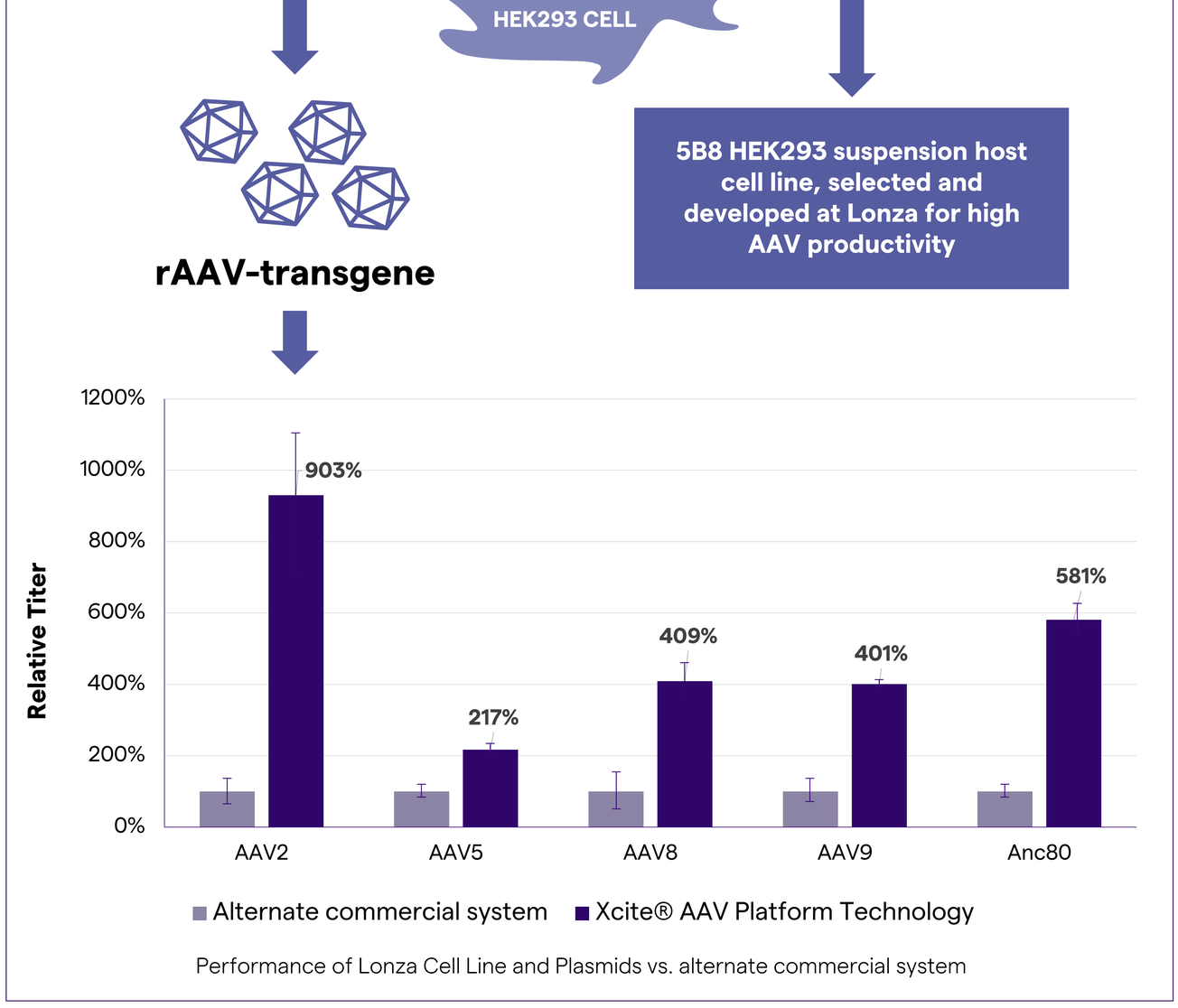
Introduction

The packaging efficiency (full to total capsid ratio, or F/T ratio) for Adeno-Associated Virus (AAV) is a critical quality attribute for the manufacturing and commercialization of AAV-based gene therapies. A higher F/T ratio has the potential for reducing dosage and eventually the cost of goods (COGS). In this study, we present design improvements in pHelper and pRepCap plasmids that can support increased AAV titers, whilst improving F/T ratio in upstream crude harvest using a triple plasmid transfection process. Data below shows significant performance improvement. This study demonstrates that we can significantly increase the AAV productivity and packaging efficiency for various AAV serotypes and client-specific Gene of Interest (GOIs) at the upstream production stage through plasmid engineering approaches.

Xcite® AAV platform technology

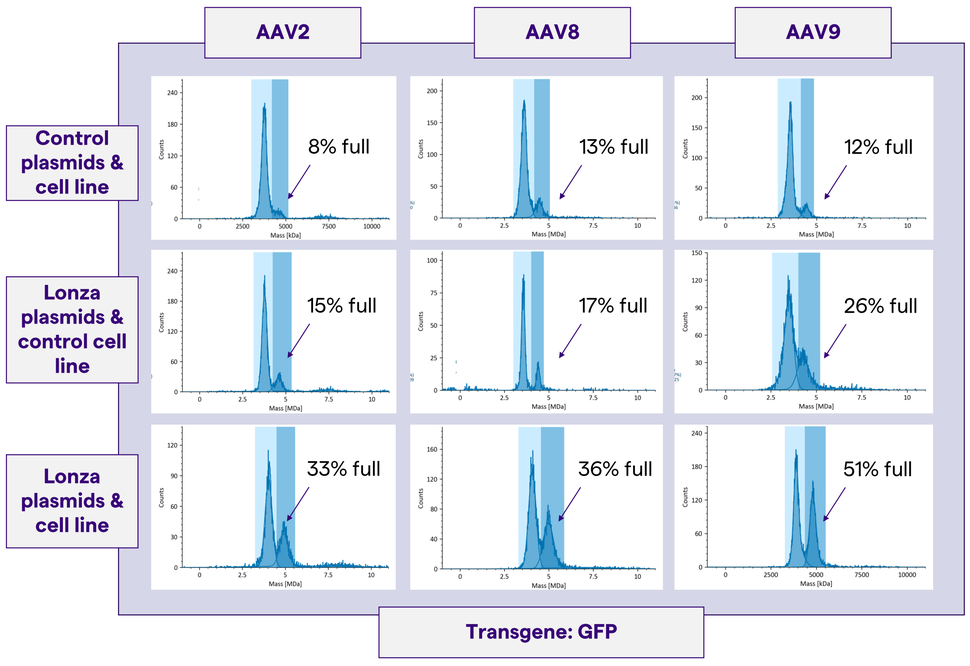
AAV-based therapies require a scalable GMP manufacturing platform that is robust and can support high titers during production. Traditionally AAV manufacturing for gene therapy entailed the use of labor-intensive adherent-based HEK293 processes not amenable to scale-up. Suspension adaptation of HEK293 cells has enabled more scalable processes but remains time-consuming. Low AAV productivity and lack of platform processes continue to be key challenges driving AAV production cost up. In response to these challenges, Lonza has established a robust and scalable suspension manufacturing platform for AAV production.

Lonza's Xcite® AAV platform process is our proprietary HEK293 Host Cell Line (5B8) and AAV Production Plasmids. The 5B8 cell line is a HEK293 suspension host cell line, selected and developed at Lonza for high AAV productivity. The 5B8 cell line is cultured in animal-component-free conditions and has demonstrated high expression and scalability for AAV production. Research and cGMP cell banks are available, under license, to take to your laboratory. The cell line productivity is further boosted by Lonza's proprietary Helper and RepCap plasmids (patent pending) across multiple AAV serotypes and genes of interest (GOIs). The 5B8 cell line and know-how for production of Lonza's Helper plasmid and Rep/Cap promoter are now also available to license for use in your laboratory or production facility.



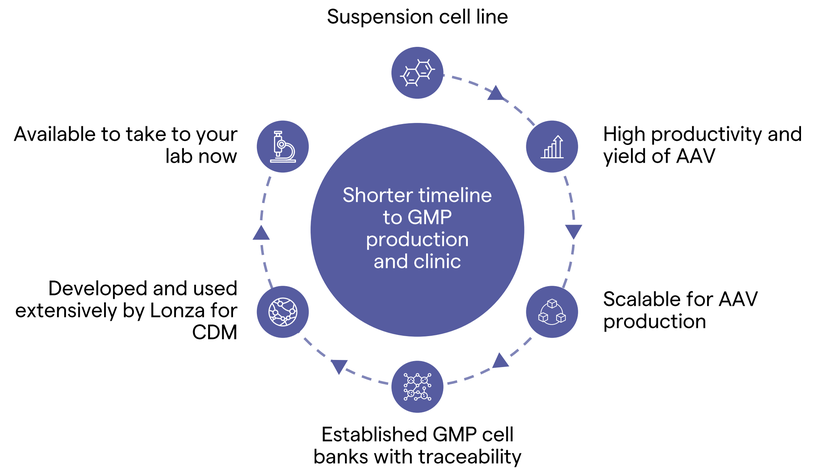
Performance of Lonza Cell Line and Plasmids vs. alternate commercial system

Xcite® AAV transient transfection system drives significantly improved full to empty capsid ratios



Consistent improvement in F/E ratio seen with Xcite® AAV system over different serotypes especially in low productivity cases

Key features and benefits – 5B8 HEK293 cell line



Lonza in Your Lab®

Research Licenses

- Covers all pre-clinical work
- Enables creating an unlimited number of cell lines*
- A complete package including access to relevant host, plasmids and an extensive know how with expert support.

Commercial Licenses

- Flexible approaches to commercial terms
- A portable system for work in-house or at partners and a range of service providers
- Favorable terms for manufacturing at Lonza*

For more details and to access Lonza's AAV Platform, contact us at licensing@lonza.com

*Subject to the terms and conditions of the license agreement

Conclusion

- Lonza cell line and plasmid system significantly improves full vs. empty ratio compared to commercial standard. Higher full ratio reduces burden on downstream processing and leads to improved final product purity – lower capsid load especially for high doses leading to improved safety profile.
- Scientists can have access to Xcite® AAV platform technology under a research license.
- Gene therapy developers can therefore benefit greatly from not only the technologies independently, but also Lonza's experience and deep knowledge regarding rAAV process development and optimization.
- Partnering with Lonza allows access to technologies and expertise that will help improve the manufacturing productivity and scalability of AAV-based gene therapies and could potentially accelerate time to clinic and market for these life changing treatments.