FASTFACTS

Driving the viral vector expressway: speeding through AAV manufacturing

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Optimized, scalable upstream production platforms are paramount in reducing the time it takes for gene therapies to reach patients. Here, we demonstrate how the VirusExpress® 293 AAV Production Platform can improve performance to achieve higher AAV titers overall, as well as the platform's ability to produce AAV2, AAV5, AAV6, and AAV9 specifically.

TRANSFECTION OPTIMIZATION FOR AAV2

As part of transfection optimization, a response surface design was used to generate a model to identify optimal transfection conditions **(Figure 1)**. This identified transfection conditions that resulted in a 60% increase in genome titers compared to baseline conditions. Additional optimization of transfection conditions was completed using alternate transfection reagents.

SCALING UP OPTIMAL AAV2 CONDITIONS

After completing transfection optimization in the Ambr 15 bioreactor, optimal conditions were scaled up to the Mobius® 3L bioreactor **(Figure 2)**. Increased genome titers were found in the Mobius 3L when compared to the Ambr 15, with a 3× improvement from the earlier baseline conditions.

TESTING OTHER SEROTYPES: AAV5, AAV6 AND AAV9

To demonstrate the applicability of the VirusExpress Production Platform to other AAV serotypes, transfection improvement learnings from AAV2 were applied to AAV5 and AAV6 production. This resulted in a 50–60% increase in genome titer **(Figure 3)**.

A process development project for a client was performed using AAV9 **(Figure 4)**. The mixture space of AAV9 plasmids was characterized using the Ambr 15 and the plasmid ratio that maximized genome titer was identified. A scale-up of the top conditions was then performed in the Mobius 3L bioreactor. As previously found with AAV2, increased genome titer was found in the Mobius 3L bioreactor when compared to the Ambr 15.

Figure 2. AAV2 production using the VirusExpress AAV platform in the Ambr 15 and Mobius 3L bioreactors.

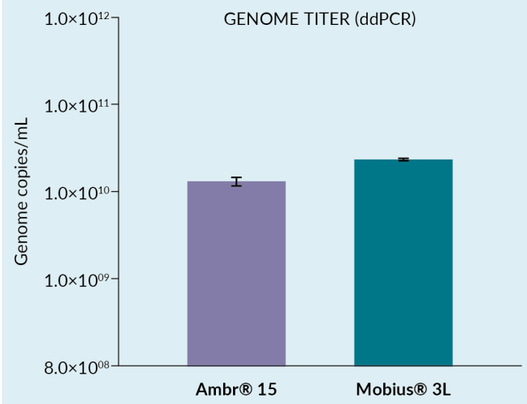


Figure 3. Application data of VirusExpress Platform for AAV5 and AAV6.

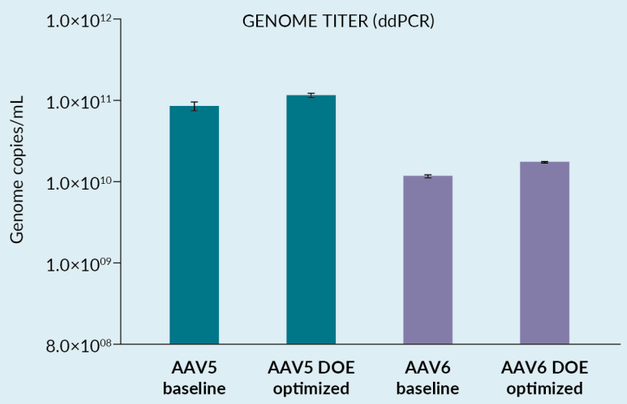


Figure 1. VirusExpress AAV Production Platform transfection optimization for AAV2 production in the Ambr® 15 bioreactor using response surface design of experiment (DOE).

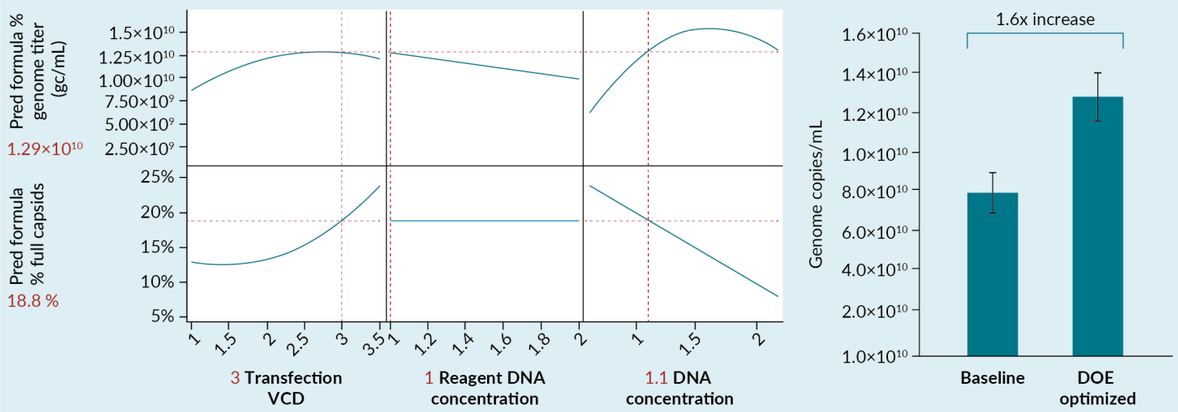
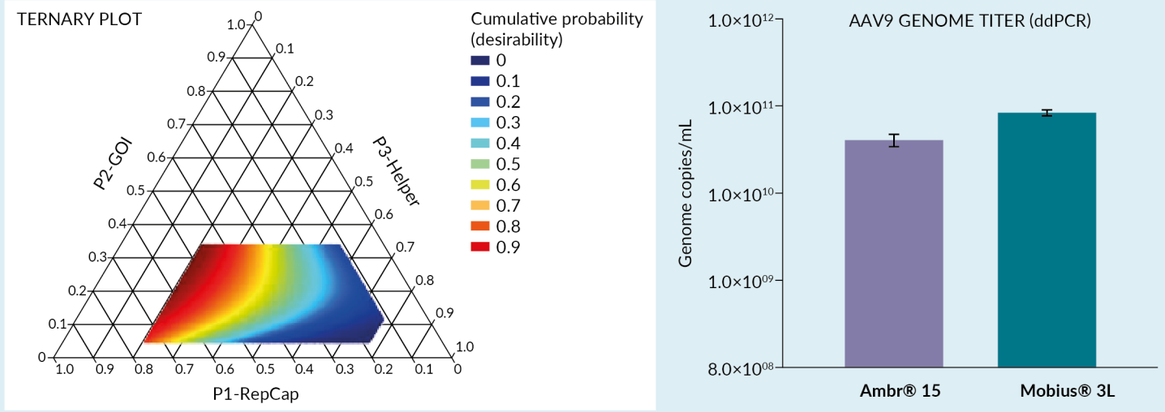


Figure 4. Application data of VirusExpress Platform for AAV9.



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