DEVELOPING A SUSPENSION TRANSFECTION PLATFORM TO PRODUCE ADENO-ASSOCIATED VIRUSES

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Key Words: AAV Vectors, Vector Production, Suspension, Process Scale-up, QbD

Through the delivery of recombinant adeno-associated virus (rAAV) vectors, gene therapy has the potential to cure and/or treat many genetic disorders. Currently, most rAAV vector production processes employ triple transfection in an adherent production vessel, which has limited scalability that results in a low batch yield. Improving process yield is critical for enabling the treatment of large disease indications and lowering manufacturing costs. One way to increase rAAV vector production is to employ suspension cell culture, which would allow for a larger process scale. In this work, through optimization of transfection and process parameters, we demonstrate a significant productivity improvement over our previously established suspension transfection process. We took a Quality-by-Design (QbD) approach to explore the transfection and process parameters utilizing multi-factor Design of Experiments (DoEs). The DoE model established in the Ambr250 accurately predicted upstream productivity in the scaled up 2 L and 50 L bioreactor systems. With a clinically relevant product, this process has demonstrated the potential to yield >1e14 GC/L. By increasing single-batch productivity by >10-fold from a comparable adherent process, this process significantly decreases the timeline for gene therapy treatments.