SCALE UP OF SF9/BEVS-BSED AAV PRODUCTION PROCESS FOR GMP-MANUFACTURING OF CARDIOVASCULAR GENE THERAPIES

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Adeno-associated virus (AAV) gene therapy (GT) has become a safe and effective therapeutic modality for patients suffering from genetic diseases. One of the key challenges to this modality, however, is designing manufacturing process with consistent quality and yield, as well as scalability that meets the scale of potential drug product demand for a patient population.

There are multiple manufacturing platforms for AAV GT, with two well-established manufacturing platforms, Sf9/recombinant baculovirus system and triple transient transfection using HEK293, that are widely used in both clinical and commercial scale manufacturing. The triple transient transfection using HEK293 can rapidly supply AAV vectors for research and early-stage clinical trials, however, due to its limitations with scalability and yield, it is not yet proven feasible for larger scale manufacturing for non-ultra-rare disease indications.

At Tenaya, we are working on developing the next generation cardiovascular therapies, including using AAV to potentially bring curative treatments to patients suffering from genetic form of heart diseases such as hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC). In this work, we report a successful scale up of the Sf9/BEVS-based AAV production process from pilot (200 L) to manufacturing scale (1,000 L) while maintaining a comparable yield and product quality. We also present a case study of a successful tech transfer of the AAV production process to Tenaya's Genetic Medicines Manufacturing Center (GMMC) - Tenaya's newly commissioned in-house GMP manufacturing facility. The facility has completed its first GMP 1000L-campaign and is fully operational in supporting clinical and commercial manufacturing of Tenaya AAV gene therapy programs.