NOVEL CELL ENGINEERING PLATFORM FOR IMPROVING PRODUCTION OF AAV FOR GENE THERAPY APPLICATIONS

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Adeno-associated virus (AAV) has emerged as a therapeutic modality in gene therapy. While there is increasing demand for viral-vector-based gene therapy, there remain bottlenecks and challenges in the virus manufacturing space. Two major challenges include low yields and low ratios of full to empty capsids. Here we present a novel cell engineering platform based on the creation of homotypic HEK-293 cell hybrids to meet these challenges. After several rounds of cell fusions followed by selection, pools as well as cell clones were evaluated for AAV production by transient transfection. This directed evolution strategy yielded a 3-fold productivity improvement (up to 10^{13} vg/L) and an improved full-to-empty ratio compared to un-engineered cells. This use of host-cell hybrids to generate and exploit genetic diversity should be applicable to production of other viruses as well.