IMPROVING RECOMBINANT ADENO-ASSOCIATED VIRUS PRODUCTION THROUGH PLASMID DESIGN AND HOST CELL LINE OPTIMIZAITON

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Recombinant Adeno-Associated Virus (rAAV) has evolved to be the most used delivery system for in vivo gene therapy due to its safety profile and long-term transgene expression. One primary platform for rAAV production uses transient transfection, in which the gene of interest and viral elements necessary for rAAV replication and assembly are introduced on 2-3 plasmids into the HEK293 cells in production but not integrated into the host genome. The simplicity of this platform in early development offers speed to clinic, however, efforts should be taken to improve the productivity and scalability to support clinical and commercial stage demands rather than switching production platforms at the risk of product quality impacts. Therefore, it is important to design and control critical biological materials, i.e., plasmid DNA and the HEK293 host cell line, with the final process in mind. This presentation will explore considerations for host cell line optimization for manufacturability. It will also reveal the impacts of small changes in plasmid design on not only the productivity but also the product quality of rAAV production using suspension transient transfection.

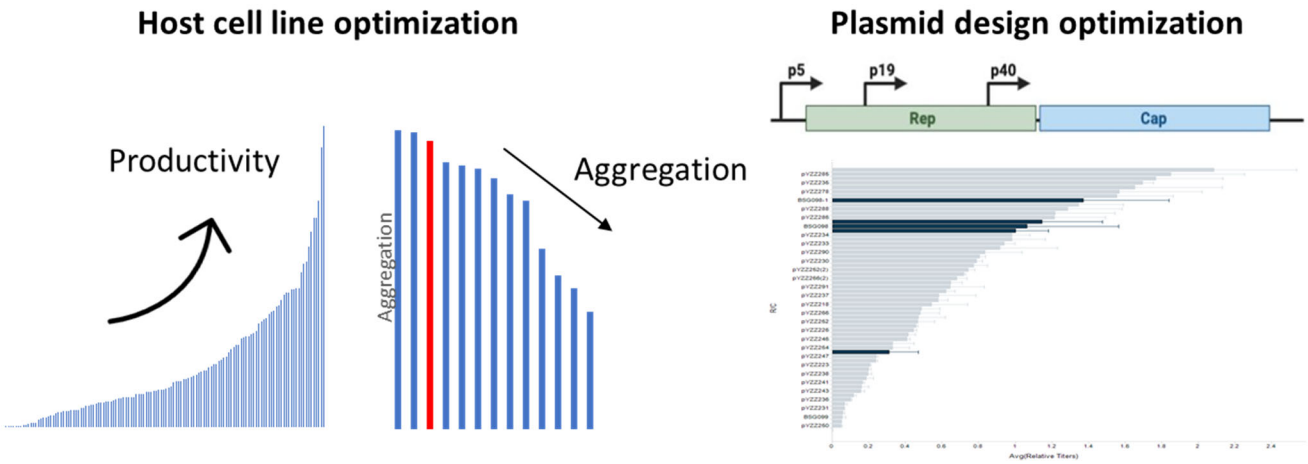

Figure 1 – Optimization of host cell line and plasmid design to improve rAAV production using transient transfection