Development of unfolded protein response (UPR) modulated HEK293 cells for improved recombinant Adeno-associated virus (AAV) production

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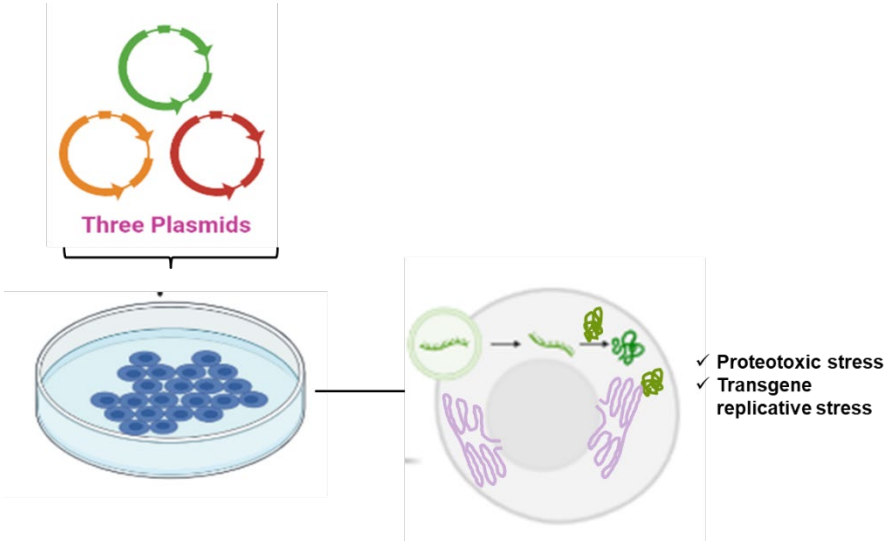
3

Graphical Abstract/ Layout



Project Description

Recombinant protein producing cells such as HEK293, CHO, BHK encounter proteotoxicity in the form of endoplasmic reticulum stress (ER stress). This could deregulate cellular homeostasis thereby limiting the transgene expression and ultimately limiting the yield of recombinant protein production. Similarly, during recombinant Adeno-associated virus (rAAV) packaging by the standard triple transfection method, HEK293 cells could undergo proteotoxicity in the form of ER stress and transgene replicative stress that potentially limits AAV packaging. The production levels of rAAV in HEK293 based systems are 10^3 to 2×10^4vg per cell. The total yield being $1 – 2 \times 10^{12}$ vg per 40 (150mm) culture dishes in lab scale. Consistency of this low yield is also an issue because of empty AAV capsids production. Eventually, the cost of rAAV production remains high. Here, we propose to identify/modulate proteotoxic stress in AAV packaging cells that impedes rAAV yield.