TESSA technology: a new paradigm in AAV manufacturing

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The majority of adeno-associated viral (AAV) vector produced globally is manufactured using triple transfection. But plasmid-based AAV manufacture has drawbacks – the need to transfect cells results in a process which cannot be truly scalable, and yield and particle infectivity could be improved upon. Tetracycline Enabled Self Silencing Adenovirus (TESSA) technology utilizes adenovirus to manufacture AAV in order to achieve reproducible AAV yields at scale with considerable cost savings. Additionally, increased vector quality and infectivity has the potential to deliver safer gene therapies at a lower effective dose.

ROBUST AND REPRODUCIBLE YIELDS

In nature, the AAV produced by adenovirus is more infectious, with considerably higher yields, than what is produced via manufacture. By harnessing adenovirus-based production of AAV and solving the issue of contamination, TESSA Technology increases AAV2, AAV5, AAV6 and AAV9 yields by >30-fold (Figure 1). For AAV2, particle infectivity is increased by >2,420-fold (Figure 2) and full:empty ratio is increased from 5 to 70%. Adenoviral contamination levels are reduced by 99.99999–100%.

REDUCED COST

TESSA technology represents a highly scalable platform for AAV manufacture which requires relatively small amounts of virus to operate, and requires only existing AAV particles in combination with one TESSA vector. Therefore, moving away from plasmid-based manufacture leads to reduced cost of goods (COG).

Figure 1

AAV2 genome yield using TESSA vectors is increased 42-fold versus a helper-free approach.

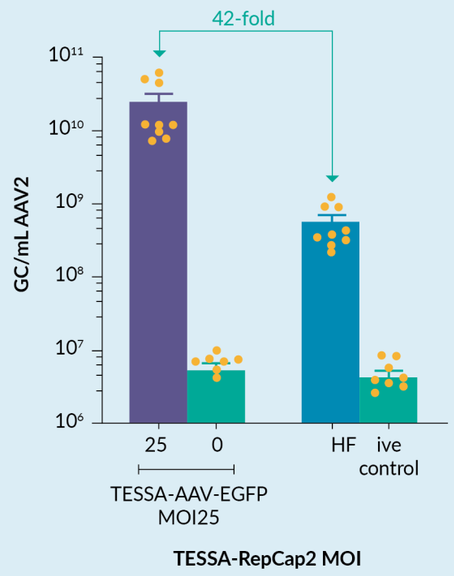
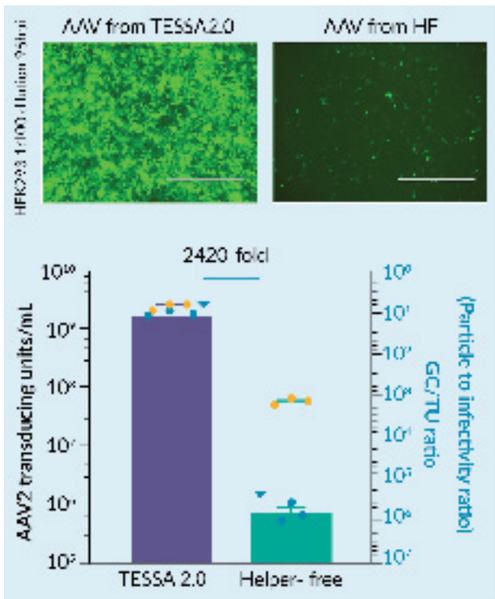


Figure 2

A 2420-fold cumulative increase in AAV2 infectious yield is seen using TESSA versus a helper-free approach.



SAFE AND EFFECTIVE GENE THERAPY

The large increase in AAV2 infectivity has important safety implications. 1 in 6 particles containing a genome are infectious when using TESSA technology, compared to just 1 in 1,200 when using plasmid-based manufacture. As AAV particles manufactured using TESSA technology are more potent, it's possible that this will lower the effective dose of AAV based gene therapies. This represents a considerable safety advantage and demonstrates that TESSA technology has the potential to produce safer and more effective gene therapies.

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