Affinia's proprietary AAV plasmid design produces industry-leading manufacturability of novel and WT capsids

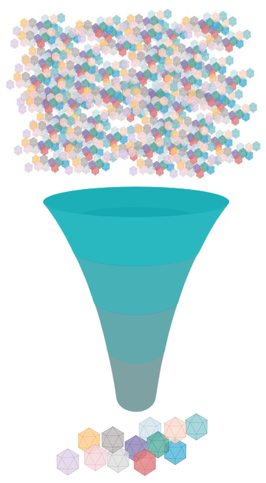
Matt Edwards, Michael White, Paul Freeman, Esther Aribilola, Matt Bennett, Patrick Bresnahan, Rong Cong, Hanna Czeladko, Spencer Fiedler, Ramin Kamran-Sami, Graham Lilley, Shahrzad Parker, Jordan Shufro, Rob May

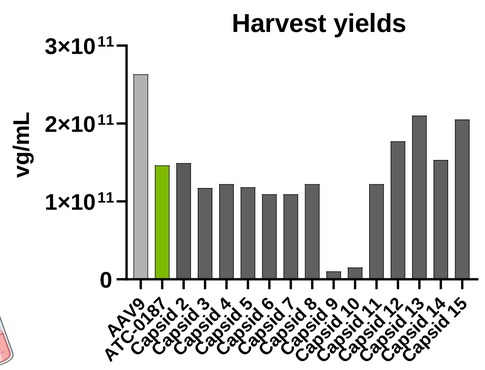
Abstract

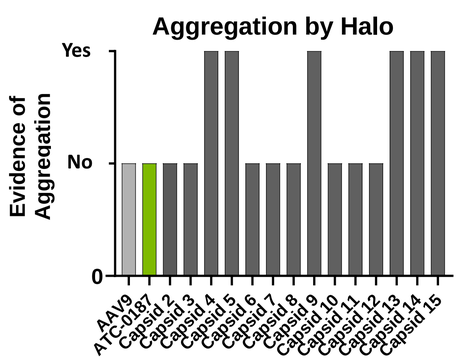
Identification of novel AAV capsids with improved tropism will unlock many additional indications for gene therapy. While the increased tropism may result in lower doses, there is still a need to have increased yields and packaging efficiency to ensure a robust, scalable manufacturing process with a lower cost per dose. We have found that performing a manufacturing assessment for yield, process fit and stability during the lead identification stage in screening leads to more commercially viable capsids arising from the screen. Here we will show data from these manufacturability screens for our myotropic and BBB-penetrant capsids. This data gives us confidence that our lead capsids will perform well as they progress into clinical development. Additionally, we have developed a robust process development toolbox that can further improve yields, packaging efficiency and stability.

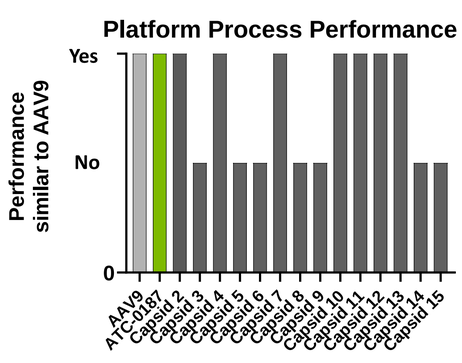
Our proprietary plasmid design increases our yields and packaging efficiency (% full capsids at harvest) for all novel capsids with peptide inserts and WT serotypes tested to date. Interestingly, we have seen that this plasmid design improves yield, packaging efficiency and residual DNA of novel capsids better than AAV9. For novel capsids we can achieve yields greater than 3e12 vg/mL and packaging efficiency over 60% while for AAV9 we can achieve yields greater than 4e12 vg/mL but packaging efficiency of only greater than 40%. Our proprietary plasmid designs lead to industry leading yields and packaging efficiency for our novel, peptide insert capsids.

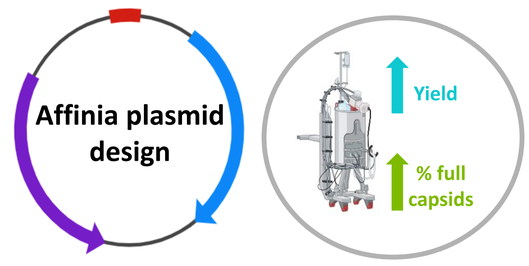
Performing manufacturability assessment of novel capsids is a key step in screening







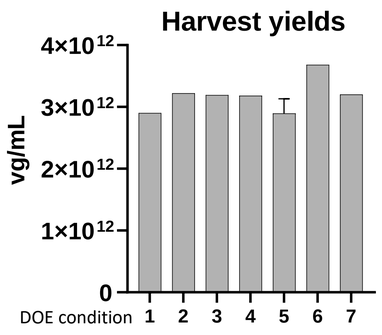


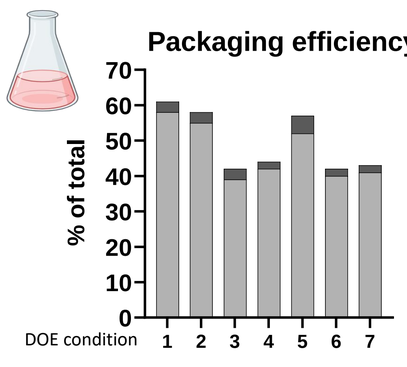


Improves yields, packaging efficiency and CQAs of any serotype with any transgene

Affinia plasmid design increases yield and packaging efficiency of novel capsids

AAV9





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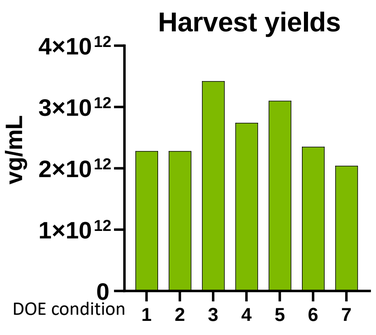

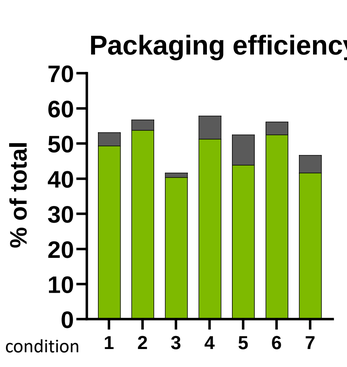

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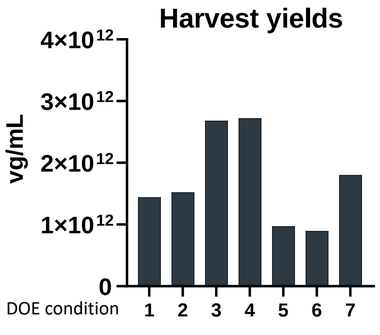
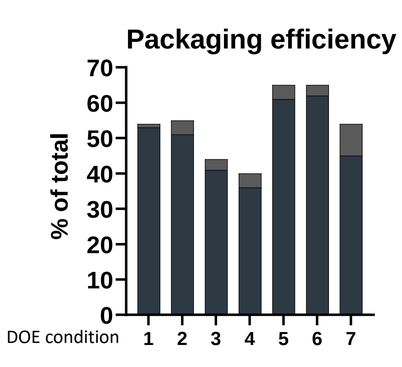
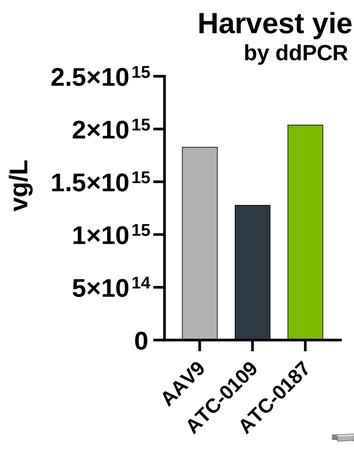
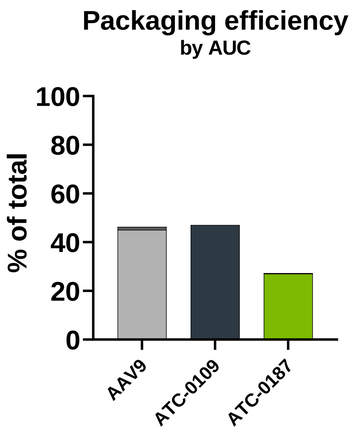




Affinia plasmid design improves yield and packaging efficiency of novel capsids

Upstream performance scales from shake flasks to 50L bioreactor and improves CQAs

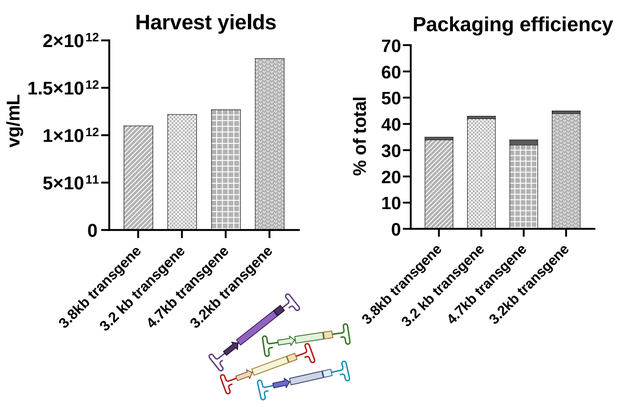




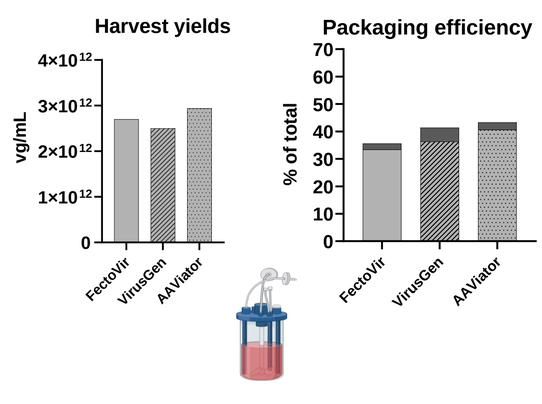
Attribute	Affinia Plasmid Design	Standard Plasmid Design
hcDNA	5-10x reduction	<10pg per 1e9 vg
Residual plasmid DNA	5-10x reduction	E10 per 1e13 vg
Infectivity / In vivo potency	No change	N/A
rcAAV	2-3 log improvement	Negative at 1e11, 1e10 and 1e9

Plasmid design works broadly within multiple processes

Affinia plasmid design works with multiple transgenes



Affinia plasmid design works with multiple transfection reagents



Conclusions

- **Manufacturability assessment during capsid selection is important to identify high quality capsids from platform screens**
- **Affinia plasmid design:**
  - ✓ **Significantly improves the yield and packaging efficiency of wild-type and novel AAVs**
  - ✓ **Scales from shake flasks to bioreactors**
  - ✓ **Significantly improves many CQAs**
  - ✓ **Works with multiple transgenes and transfection reagents**

Business Development: Alanna Murday - amurday@affiniatx.com
Process Science: Matt Edwards – medwards@affiniatx.com

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