A Small-Molecule Enhancer for Robust and Scalable rAAV Manufacturing

Enhanced rAAV productivity across vector genome sizes, serotypes, production cell lines and manufacturing scales

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P0814

From Host-Cell Modulation to More rAAV

Small-molecule enhancer — Aurora kinase inhibitor

DRIVES

Host cell modulation — Cell cycle

RESULTS IN

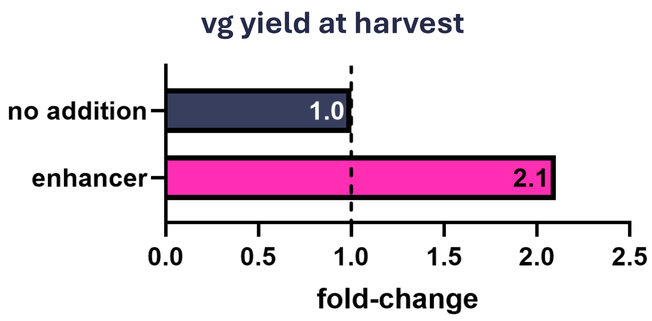
Defined cellular state — G2-M arrest

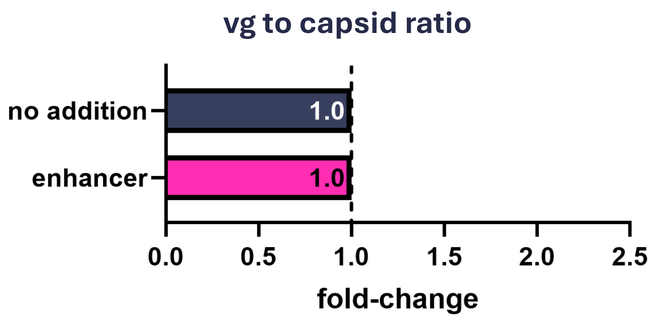
LEADS TO

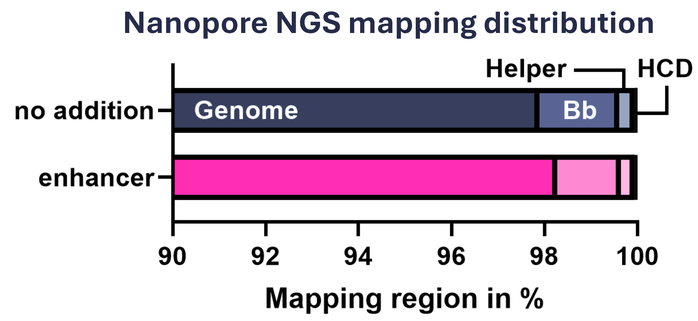
Increased rAAV productivity — More rAAV

Efficient and scalable rAAV manufacturing requires increased vector yield without compromising product quality.
We evaluated a small-molecule enhancer intended to modulate the host-cell state and improve productivity across diverse production settings.

Increased rAAV Productivity without Compromising Vector Quality





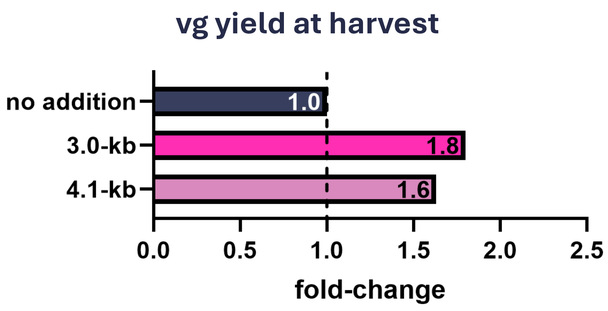


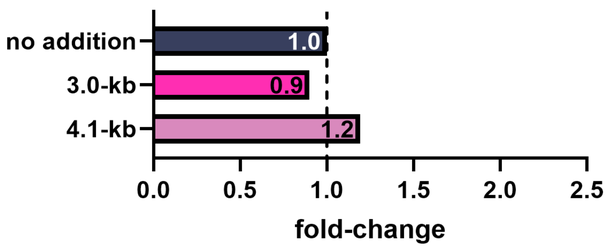
Bb: plasmid backbone, HCD: Host cell DNA

Using the Ambr15® bioreactor system, proprietary suspension HEK293 cells, and our EpyQ® dual-plasmid system, enhancer treatment increased rAAV9 vector genome (vg) yield (**2.1-fold**) while maintaining the vg to capsid ratio and Nanopore NGS mapping distribution. Thus, productivity gain is not accompanied by changes in the assessed vector-quality attributes.

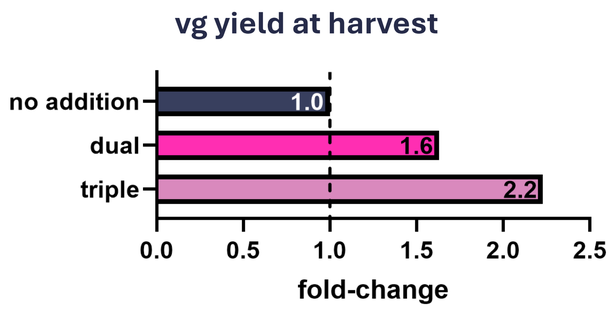
Broad Applicability and Robust Scalability

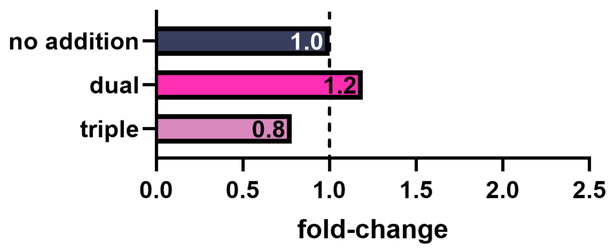
01 Vector genome size



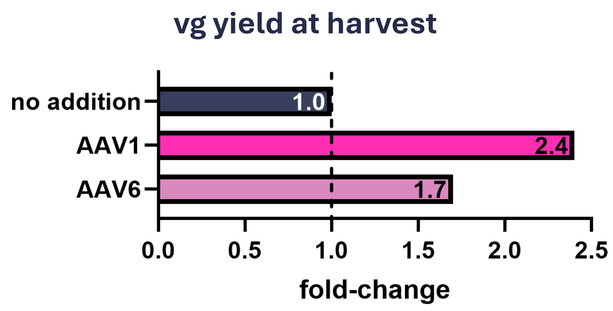


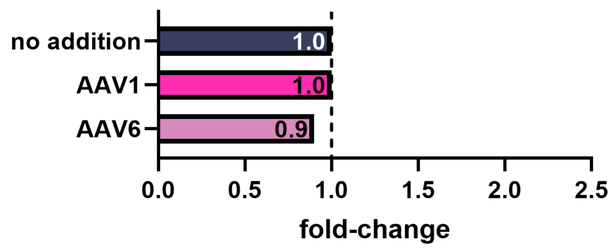
02 Plasmid system



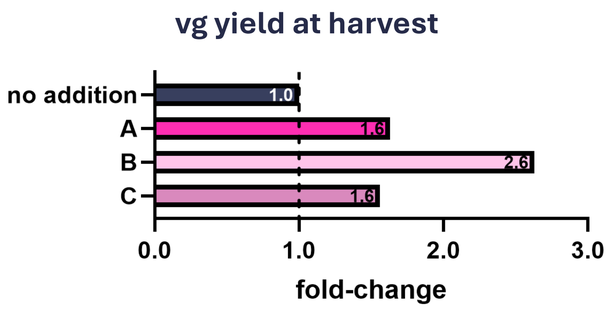


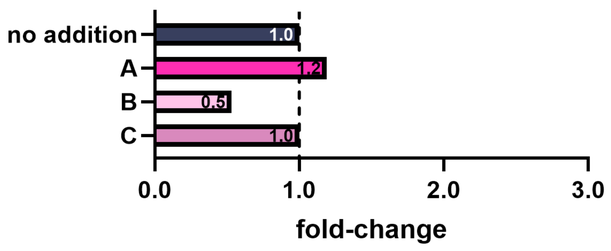
03 rAAV serotype



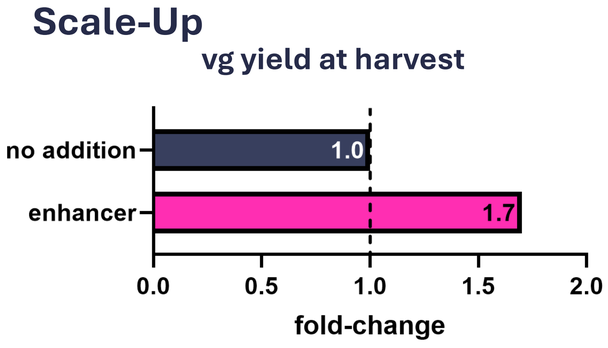


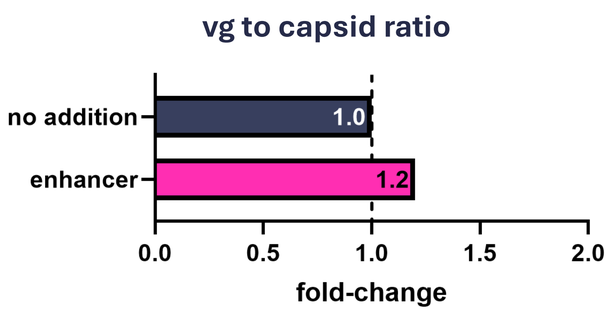
04 Production cell line





05 Scale-Up





In Ambr15 bioreactors using proprietary HEK293 cells, enhancer treatment increased rAAV2 vg yield across 3.0- and 4.1-kb vector genomes with our EpyQ plasmid system (**01**; 1.6–1.8-fold), and across both our EpyQ and a standard triple-plasmid system (**02**; 1.6–2.2-fold). With our EpyQ system, productivity gains were also observed across rAAV serotypes (**03**; 1.7–2.4-fold) and production cell lines (**04**; 1.6–2.6-fold). The vg to capsid ratio, a vector quality-related attribute, remained near the untreated reference in most conditions, although one production cell line showed a reduction.
At 5 L scale (**05**), rAAV9 production in a Biostat® bioreactor achieved a 1.7-fold increase in vg yield while maintaining a comparable vg to capsid ratio.

INCREASED Productivity (~2x)

BROAD Vector designs & capsids

ROBUST Plasmids & cell lines

SCALABLE Ambr15 to 5 L

A broadly applicable small-molecule technology for increasing rAAV productivity across vector designs, production hosts and manufacturing scales

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