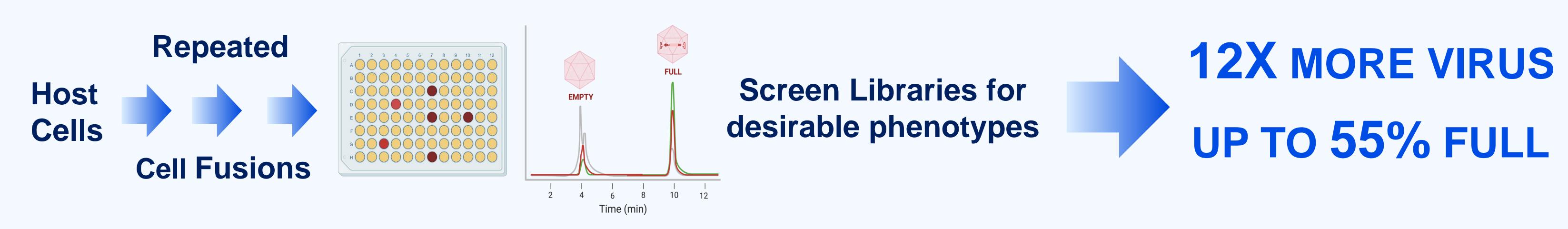
# HIGH-YIELD AAV PRODUCTION AND IMPROVED MANUFACTURABILITY ACROSS MULTIPLE SEROTYPES VIA A NOVEL CELL ENGINEERING PLATFORM

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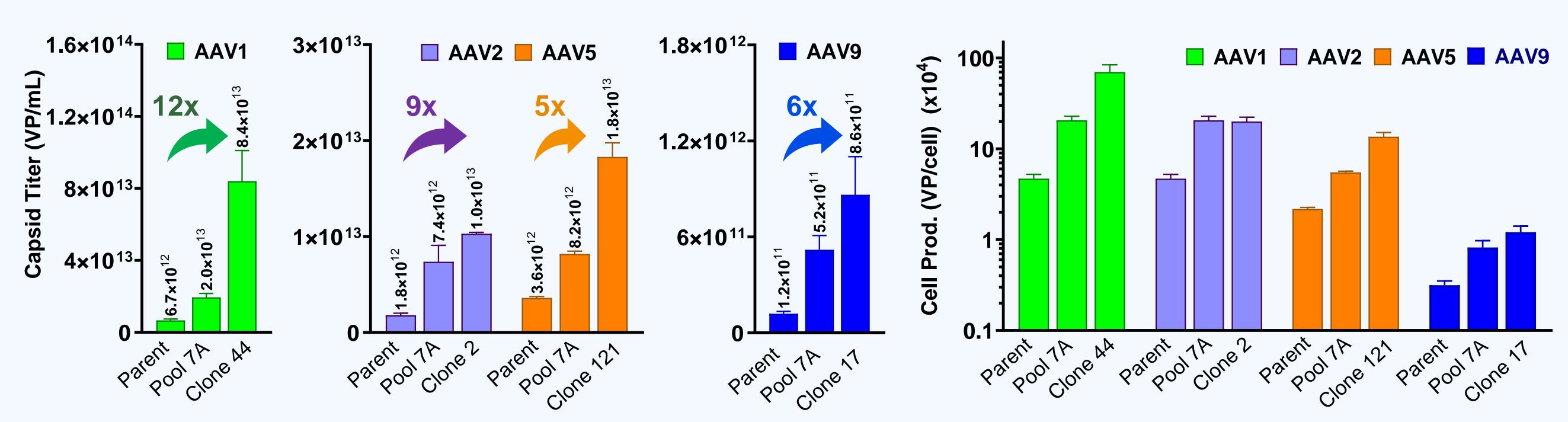
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# TECHNOLOGY PLATFORM



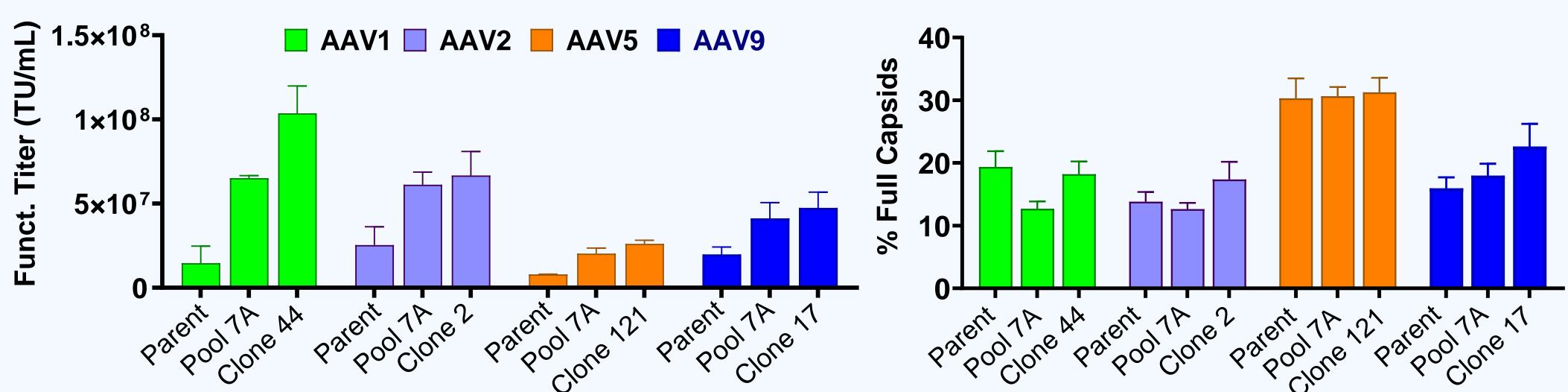
### IMPROVEMENT OF AAV PRODUCTION FOR MULTIPLE SEROTYPES

#### HIGHER PRODUCTIVITY



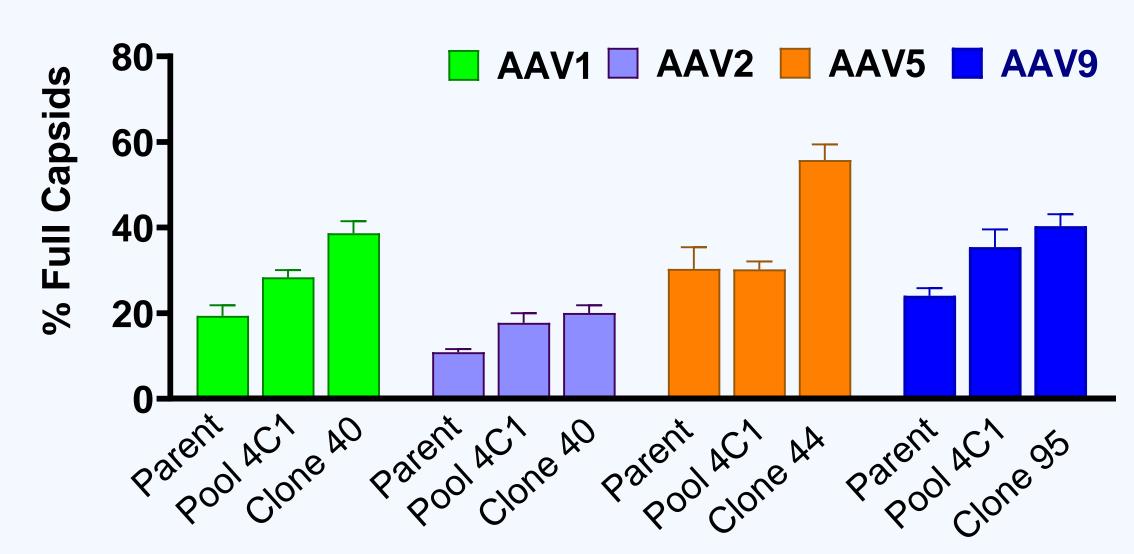
Cumulative capsid productivity (left) and specific productivity (VP/cell, right) for AAV1, AAV2, AAV5, AAV9 from HEK 293F parent, engineered pool (7A), and engineered clones. Engineered clones showed 12-fold, 9-fold, 5-fold and 6-fold increases compared to parent host, respectively. Right panel y-axis presented in log scale.

#### HIGHER FUNCTIONAL TITER AND COMPARABLE % FULL



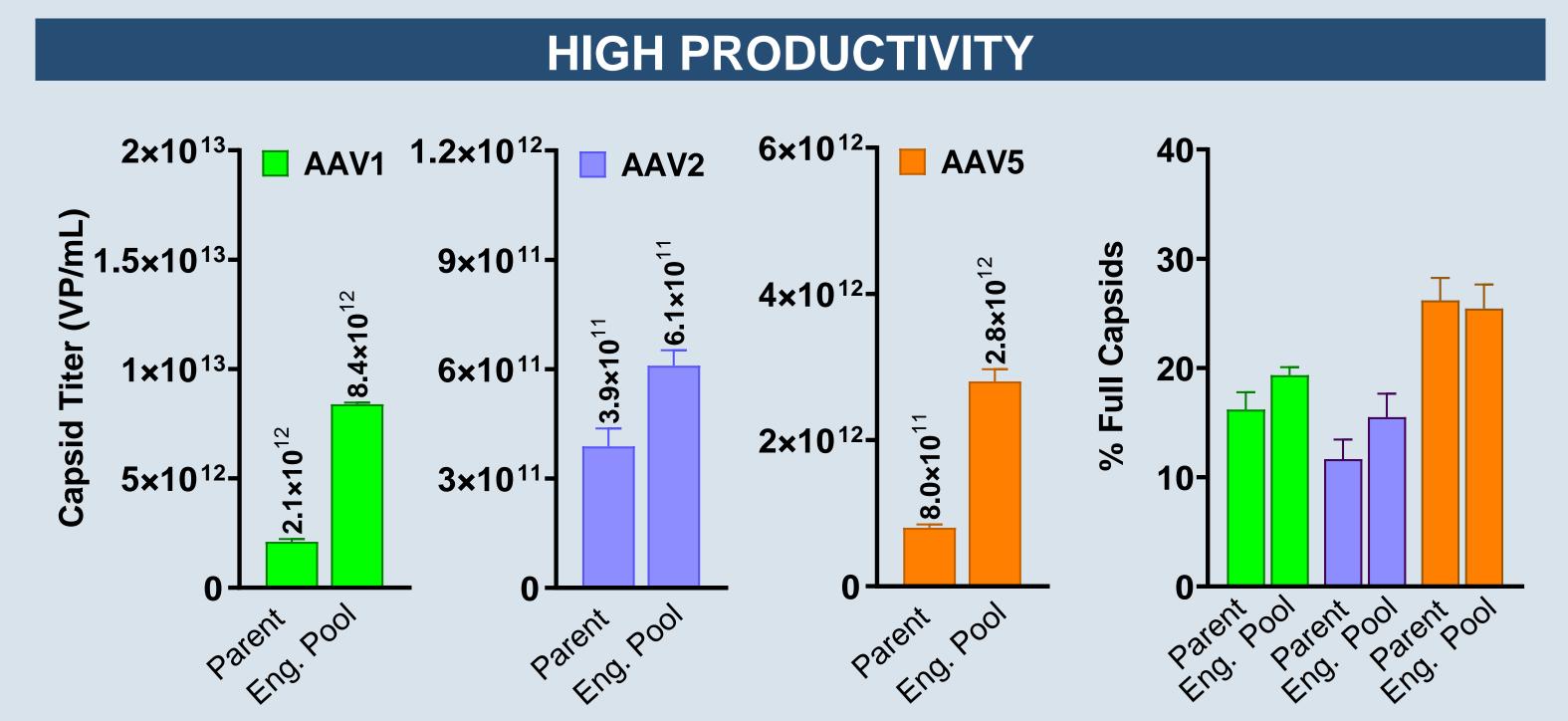
Left – AAV functional titer (measured as TU/mL) for AAV serotypes produced in HEK 293F hosts. Mean functional titer were calculated at three different virus concentrations (dilutions ranging from 1:25 to 1:300). Right –% full capsids

#### HIGHER % FULL CAPSIDS

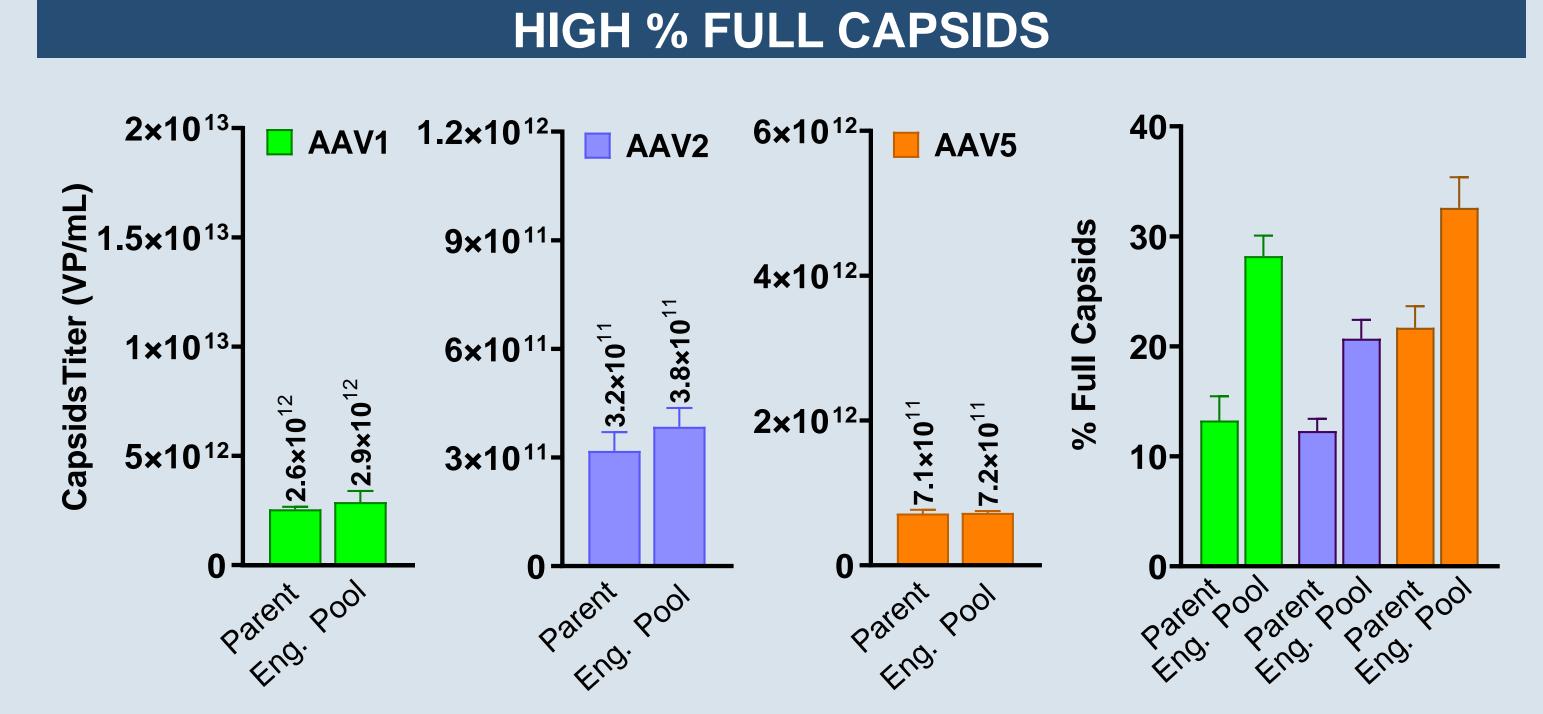


Engineered pool (4C1) and clones selected for desirable phenotypes showed a 2-fold increase in full-to-empty ratio.

## HIGHER PRODUCTIVITY AND % FULL IN STABLE PRODUCER CELL LINES (PCLs)



Capsid titer and % full capsids AAV1, AAV2, and AAV5 of producer cell line derived from HEK 293F parent or engineered pool. Producer cell lines using our system have increased capsid titer.



Capsid titer and % full capsids for AAV1, AAV2, and AAV5 from producer cell line derived from HEK 293F parent or engineered pool. Producer cell lines using our system have increased % full.

# CONCLUSIONS

We have demonstrated a disruptive cell-engineering platform to significantly improve HEK cell culture manufacturing capabilities:

- + HEK-293F cells can be engineered for up to 12-fold higher AAV productivity for multiple serotypes
- + Capsid percent-full can be increased by 2-fold, with further improvement possible
- We have developed a new system for generating high-yield PCLs in which engineered PCLs can be further engineered for higher productivity, or for higher % full capsids

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