

# New Cell Engineering Method for Increasing Recombinant Therapeutic Antibody Productivity Up To 10-Fold in Batch CHO Cultures

Kathy Ngo<sup>1</sup>, Lawrence Chasin<sup>2</sup>, Larry Forman<sup>1</sup>

<sup>1</sup>CHO Plus, Inc., South San Francisco, CA, <sup>2</sup>Columbia University, New York, NY

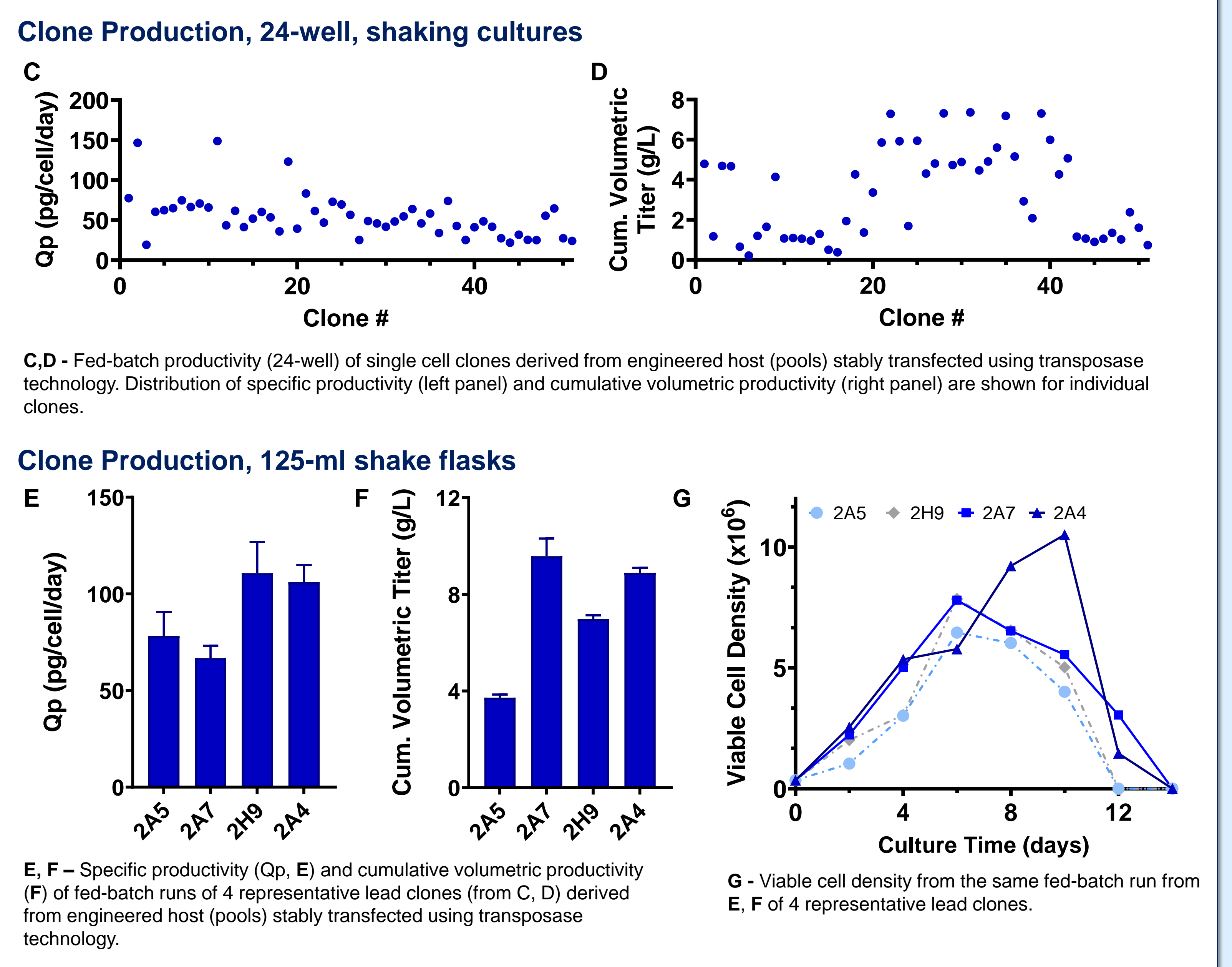
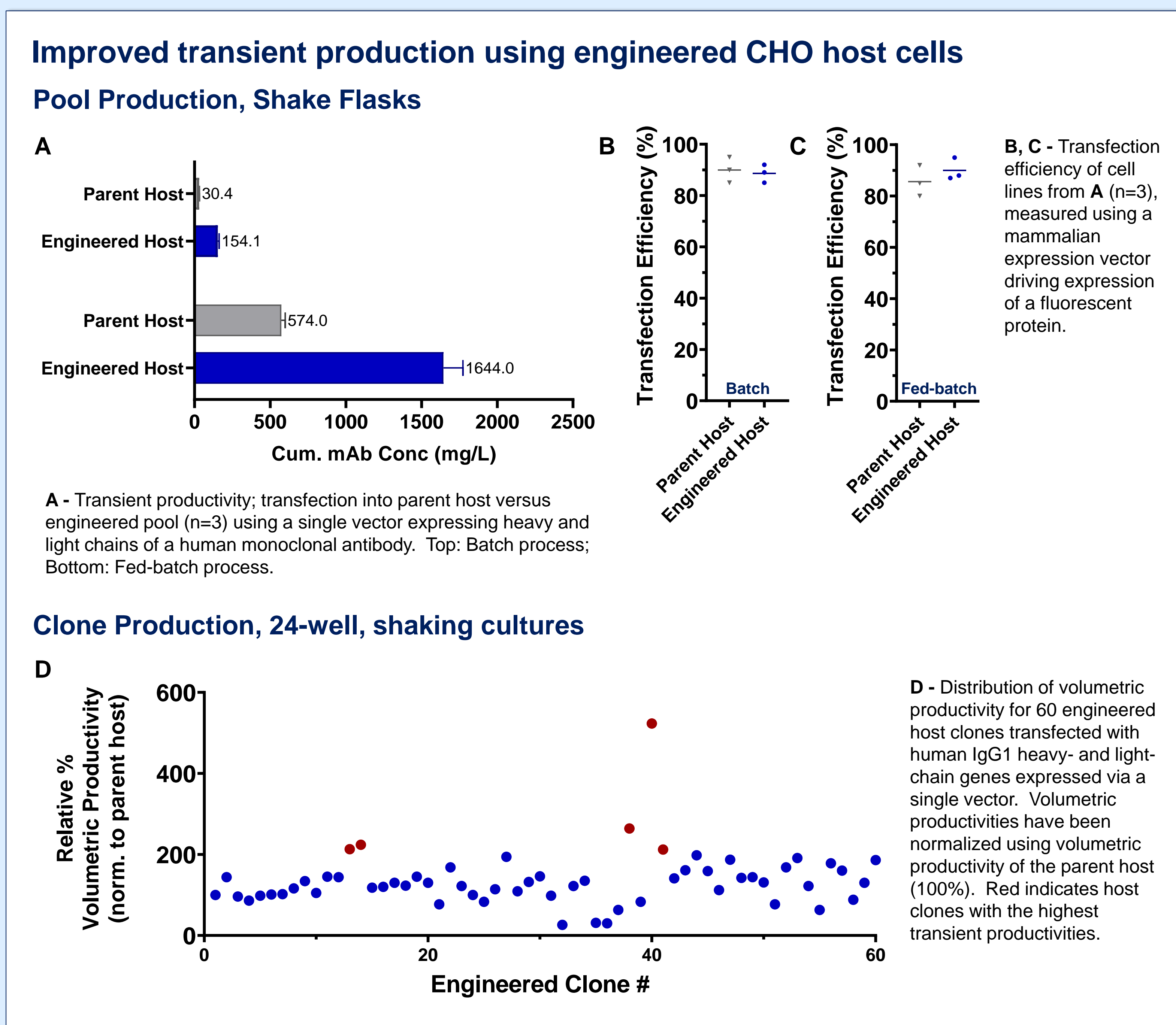
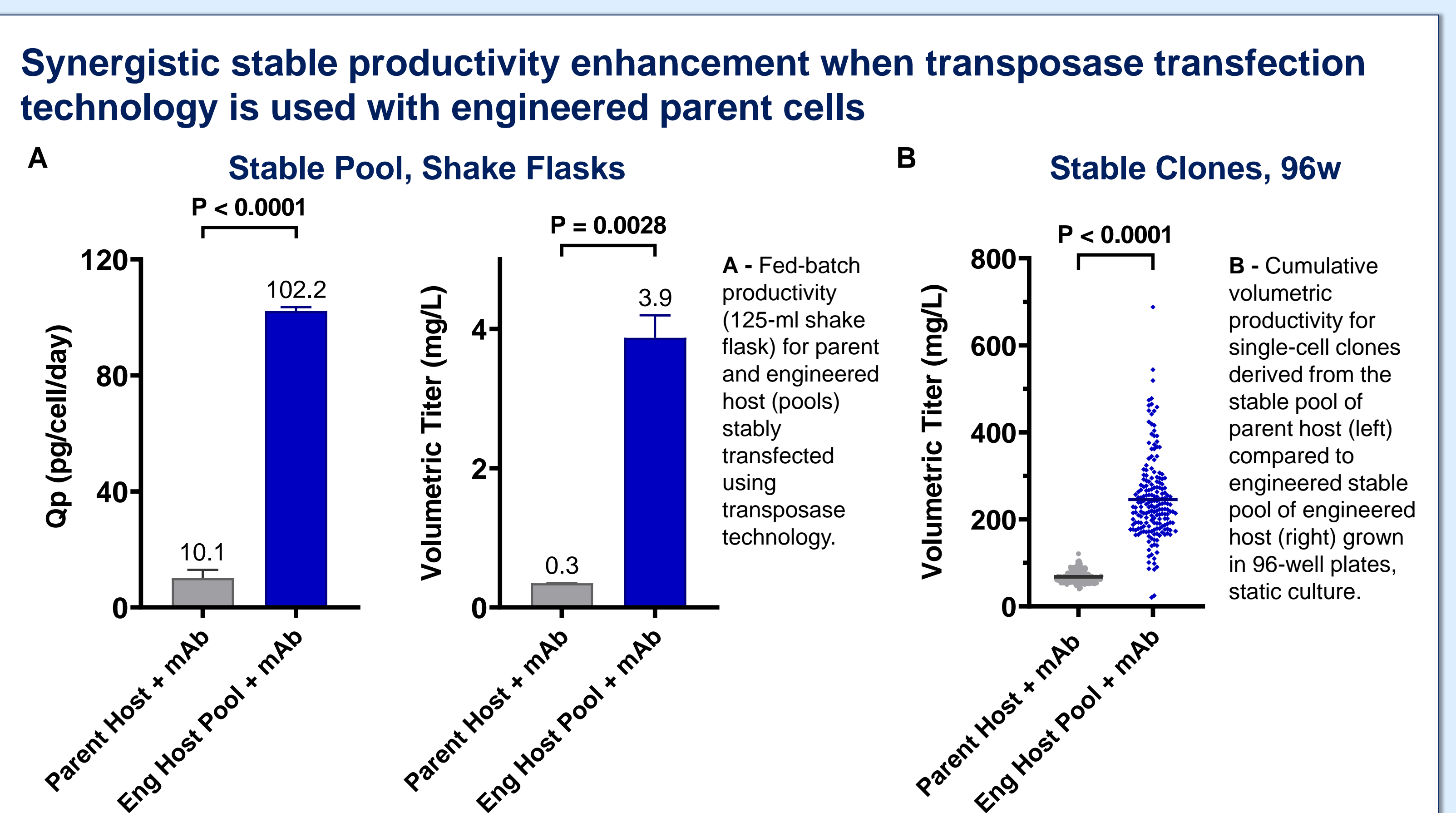
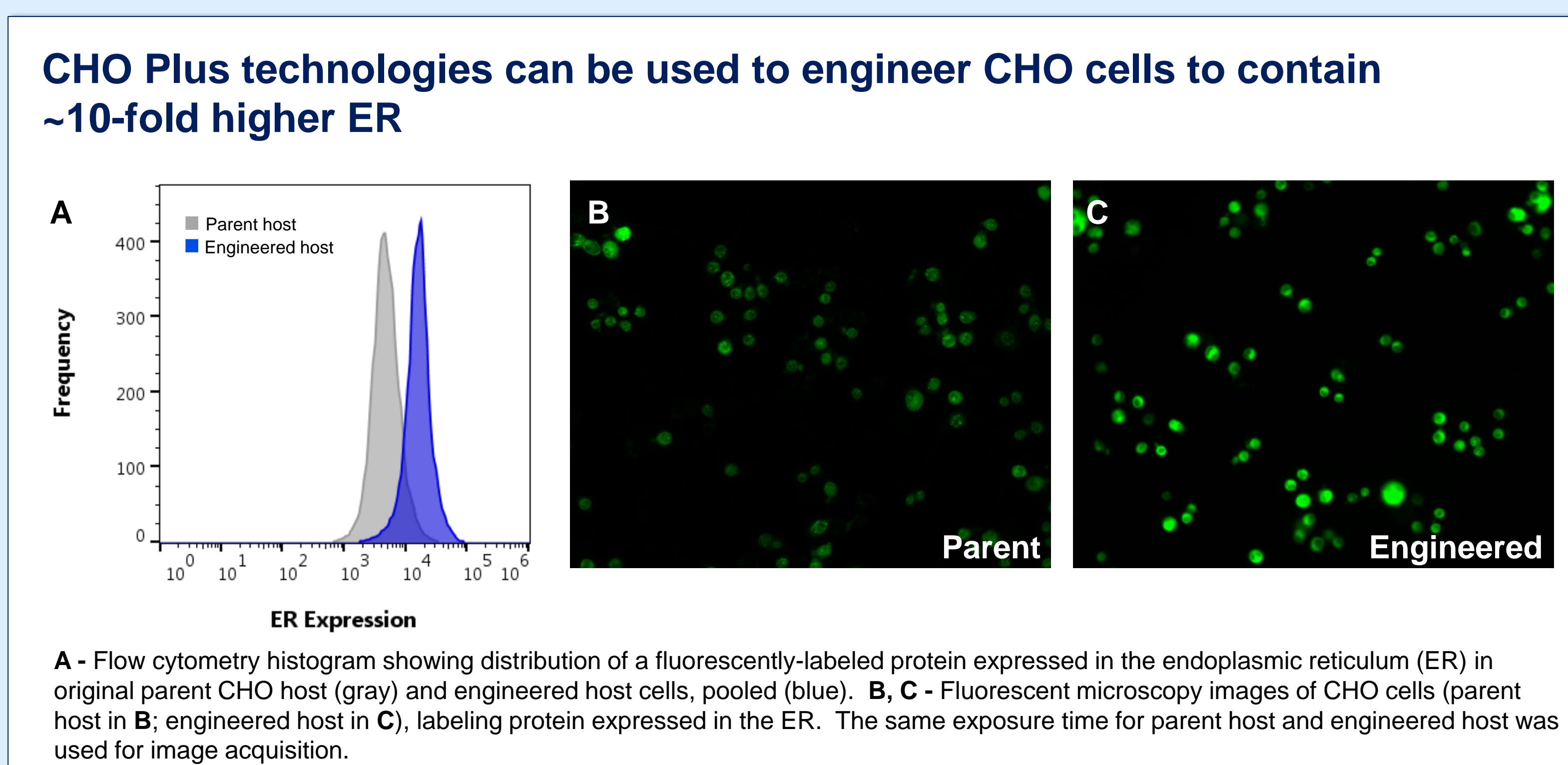
## ABSTRACT

**Background and Novelty:** Despite decades of cell culture process improvements and cell engineering methods development, there remain intrinsic bottlenecks to higher recombinant protein productivity using Chinese hamster ovary (CHO) cells. These bottlenecks limit CHO cell-based manufacturing potential. Here we disclose a directed evolution strategy to genetically engineer and select for CHO cells with enhanced protein-production machinery. CHO Plus's innovative approach circumvents natural limitations present in CHO cells, positioning it to become a new and vastly improved manufacturing paradigm for recombinant therapeutic protein production.

**Experimental Approach:** Homotypic fusions of CHO cells were selected for high expression of proteins associated with endoplasmic reticulum (ER). Fused cell hybrids advantageously selected for enhanced ER (up to >10-fold higher) were evaluated for recombinant protein production by transient and stable transfection of heavy- and light-chain genes coding for a recombinant human therapeutic monoclonal antibody (mAb).

**Results and Discussion:** CHO cells engineered using our approach exhibited enhanced transient specific and volumetric productivities for a human mAb of up to 4-fold compared to un-engineered parental cells in batch cultures. For stable transfection, up to 10-fold increases were observed for specific and volumetric productivities for engineered cells expressing a human mAb at the transfected-pool stage, with clones producing mAb concentrations of up to 9.5 g/L in shake flask cultures.

CHO Plus has demonstrated that our cell engineering technologies, leveraging directed evolution methods, represent a novel and disruptive platform for vastly improving CHO cell manufacturing capabilities.



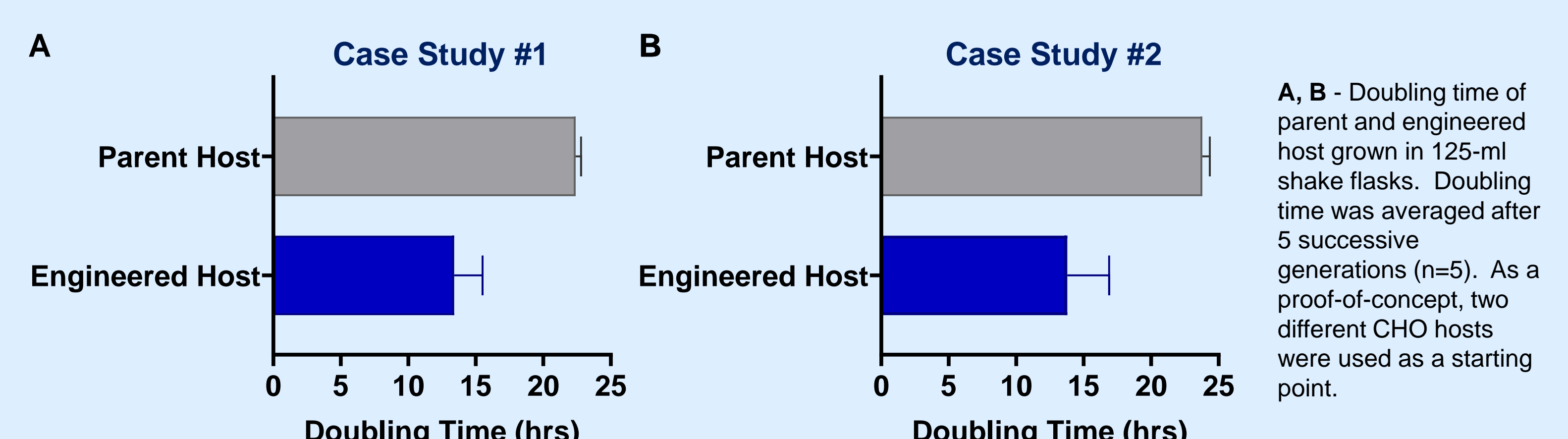
## CONCLUSION

We have demonstrated a disruptive cell engineering platform to vastly enhance CHO cell culture manufacturing capabilities:

- + Synergistic productivity enhancement in engineered cells when used with transposase technology
- + Up to 10-fold increase in productivity via transient and stable transfections
- + Up to 9.5 g/L volumetric productivity demonstrated for single-cell clones at shake flask scale
- + Additional phenotypes, such as faster growth, can be engineered into host cells
- + Cells can be engineered for faster growth; growth rate increased by 50% while maintaining initial cell-specific productivity

## OTHER CAPABILITIES

The CHO Plus cell engineering platform can be used to engineer-in additional advantageous phenotypes, such as faster growth, while maintaining productivity of the un-engineered cells:



[www.CHO-Plus.com](http://www.CHO-Plus.com)

