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Synthetic cell line for high-yield rAAV production

A synthetic cell line designed to enhance recombinant adeno-associated virus (rAAV) productivity and improve the ratio of full to empty viral particles.

IP Status: PCT Pending; PCT/US2024/025382; US Patent Pending 19/476,922

Applications

- Gene therapy vector manufacturing
- Research and development of viral vectors
- Large-scale biopharmaceutical production

Key Benefits & Differentiators

- **Higher productivity:** A novel synthetic cell line design and genetic construct enables higher rAAV titers and improved vector quality on a per-cell basis
- **Enhanced quality:** Optimized vector design enhances the yield of genome-loaded viral particles, minimizing downstream purification requirements.
- **Simplified process:** The technology streamlines the upstream production process by eliminating the need for plasmids and helper viruses

Technology Overview

The production of recombinant adeno-associated viruses (rAAVs) is critical for gene therapy applications, but current manufacturing methods face significant challenges. These issues include low rAAV titers and an unfavorable ratio of full to empty viral particles, which compromise efficiency and quality. Existing solutions often involve increasing culture volume to compensate for low titers and relying on extensive and costly downstream purification methods like ultracentrifugation or ion exchange chromatography to remove empty capsids. These workarounds fail to address the fundamental inefficiencies in the production process, leading to higher costs and complexity.

Researchers at the University of Minnesota have developed a novel synthetic cell line with stably integrated DNA sequences encoding viral proteins and a recombinant viral genome. The expression of these components is under the control of external signals, allowing for precise manipulation to maximize rAAV productivity and enhance the content of full viral particles. The technology incorporates a conditional promoter system for the recombinant genome, coordinated promoters for viral gene expression, and a method of using proteasome inhibitors to further increase rAAV titers. This comprehensive approach results in significantly higher titers of high-quality rAAVs, streamlining the upstream process and reducing the burden on purification.

Phase of Development

TRL: 3-4
A working prototype cell line has been engineered and produces virus titers comparable to current industrial methods. Optimization is underway to increase productivity.

Technology ID
2023-257

Category
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Life Sciences/Pharmaceuticals
Life Sciences/Research Tools
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Researchers

- **Wei-Shou Hu, PhD** Professor, Department Chemical Engineering and Materials Science

References

1. Min Lu, Yu-Chieh Lin, Han-Jung Kuo, Wen Cai, Qian Ye, Liang Zhao, Wei-Shou Hu(2024) , https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/biot.202400051, https://analyticalsciencejournals.onlinelibrary.wiley.com/journal/18607314, 19