Smart Notes

Which features are important considerations when evaluating a large orbital shaker for production of plasmid DNA encoding viral vectors, for applications including CAR-T, gene therapy, or other genetic engineering?

When producing plasmid DNA that encodes a virus, it's important to ensure integrity of the host bacterial culture. An orbital shaker for this purpose should provide smooth, vibration free motion, continuous and effective contamination control, simultaneous parameter entry and viewing, accessibility for cleaning, and high revolutions per minute (RPM). Together, these qualities help protect the culture and provide high yield.

In many gene therapy and cell therapy applications, whether at research scale or therapeutic production, engineered viral vectors are used to modify a target cell gene. The vector is encoded by a library of DNA plasmids, each of which holds a portion of the complete engineered viral genome. In this way, several different plasmids are required together for construction of the virus, offering quality and safety assurance.

High yields are important in any production, and speeds up to 400 RPM have been shown to produce higher yields.[1] Especially with DNA encoding viruses, limiting circulating microorganisms which could potentially contaminate the culture is important for ensuring the integrity of the final product. Similarly, features which facilitate easy, regular cleaning ensure that no surfaces will harbor residual contaminants. And the ability to simultaneously view and modify parameters while the shaker is in operation ensure quality control.

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How can orbital shaker features help ensure the best plasmid DNA product?

High yield

Maximum plasmid DNA yield is provided by ideal conditions for microbial growth including a smooth swirling action provided by a triple counterbalanced drive, over-temperature and under-temperature controls, and a high RPM speed of 400, even while units are stacked three high.[1] This requires a very robust, reliable and smooth shaking mechanism. Temperature uniformity should be verified throughout the chamber using liquid testing to ensure uniform, repeatable yields.

Contamination control

For high end applications, it is also critical to ensure that the bacterial culture remain free of contamination which could come from the surrounding air or from previously spilled cultures, which may contain DNA for a different viral vector.

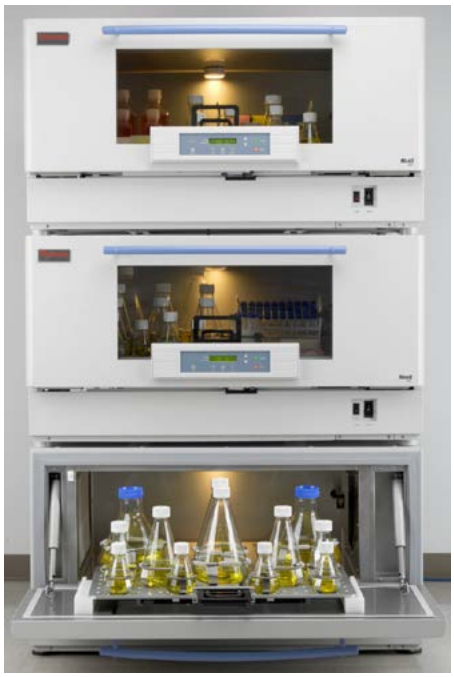

Figure 1: Thermo Scientific™ MaxQ™ 8000 Stackable Shakers offer incubation and refrigeration controls which are easily accessible even when stacked three high, and maximum RPM of 400 can be used even when stacked.

HEPA filtration – incorporated into the shaker mechanical airflow – captures airborne particles of all sizes with a minimum 99.97% efficiency, works continuously and only needs replacing once per year. HEPA filters are rated for their efficiency of capturing 0.3 µm particles because these are the least efficiently captured. Smaller and larger particles are captured even more effectively.[2]

Features facilitate cleaning and handling

The shaker platform should be easily removable to ensure that cleaning and disinfection of the shaker chamber are performed regularly.[3] The platform should be constructed of anodized aluminum and not painted, since painted surfaces can be easily scratched, offering areas that allow microorganisms to collect.

An easily accessible built-in drain and crevice-free coved corners in the stainless steel chamber make thorough cleaning even simpler.

Dual displays that allow simultaneous viewing of set and run parameters ensure that the correct conditions are always entered and observed, helping to limit data entry errors.

Summary

For production of viral vector-encoding plasmid DNA, an orbital shaker should offer features to provide high yield, contamination control, and simple cleaning and control.

References

1. Reames R, Gelinkse M, Thapa S. Optimization of plasmid DNA production in *Escherichia coli* utilizing the Thermo Scientific MaxQ 8000 incuubated stackable shakers. Thermo Fisher Scientific ANSHKE8000 0916, 2016.
2. TSI Incorporated. Mechanisms of filtration for high efficiency fibrous filters. Application Note ITI-041 Rev B, 2012.
3. Bates MK, Livingston S. Orbital shaker benchmarks: best practices for use and maintenance. ANMAXQBEST 0217 2017.

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