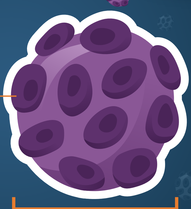
MICROCARRIER-BASED hiPSC EXPANSION

Microcarriers are microbeads capable of supporting cell adhesion and growth in a suspension culture environment.

Human induced pluripotent stem cell (hiPSC)

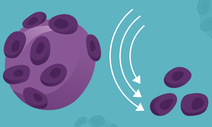


This technology provides the vast surface area required for adherent cultures to grow, combined with the advantages of a mixed suspension culture.

90-350 µm High surface-area-to-volume ratio

Merging this technology with an automated bioreactor platform such as the vertical-wheel system enables homogenous, low-shear mixing as well as process monitoring and control.

Conversely, traditional horizontal blade bioreactor systems require high agitation rates which produce small eddies, resulting in shear stress. Shear stress causes poor cell health and even detachment from the microcarrier.



In the vertical-wheel bioreactor, you can control:

- oxygen tension (pO_2)
- pH
- temperature
- agitation rate
- metabolite concentration

ADVANTAGES AND CHALLENGES OF DIFFERENT SCALING METHODS

CONVENTIONAL 2D CULTURES

Advantages

- Simple set up and maintenance
- Low-cost set up and maintenance
- Tried and tested protocols

Challenges

- Limited scale due to large footprint requirement
- Labor-intensive operation
- Often involve multiple open events, increasing contamination risk
- Limited opportunities for in-line process monitoring
- Limited control of environmental factors
- Batch-to-batch variability

MICROCARRIER-BASED SCALE UP

Advantages

- High-density cell cultures in a confined space
- Easily adjust surface area by changing microcarrier concentration
- Continuous process monitoring
- Control of environmental parameters
- Closed and controlled environment
- Reproducible, robust and scalable cell-culture processes
- Yields over 10 billion cells in one batch with high viability and stemness expression markers

Challenges

- Microcarrier clumping and cell detachment from microcarriers due to mechanical forces
- Harmful effects due to shear stress
- Difficult to harvest cells from microcarriers without an detrimental effects to differentiation capacity
- Oxygen control can be a challenge at high densities
- Increased operating costs

TIPS AND TRICKS TO OVERCOME ASSOCIATED CHALLENGES

Optimize the environmental conditions within the bioreactor.

Optimize your harvest conditions to include:

- Enzymatic treatment
- Temperature control
- Appropriate process duration
- Cell wash and concentration steps