

A HEK293 cell line for industrial production of recombinant proteins, viral vectors and vaccines

SUMMARY

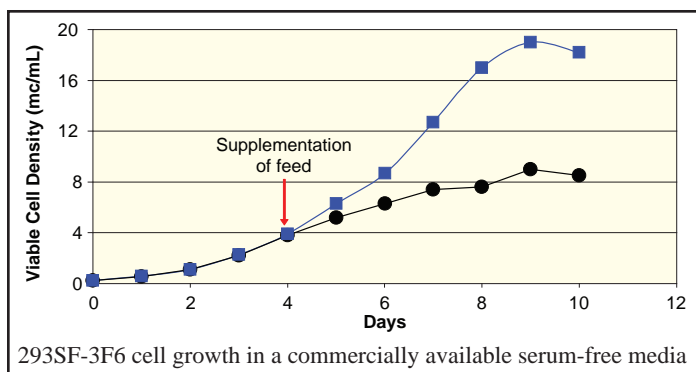
There is an increasing demand for biopharmaceuticals produced from animal cell culture processes such as vaccines, humanized monoclonal antibodies, and gene therapy products. This technology offers a solution to the requirements for the high yield production of viral vectors and vaccines and post-translationally modified recombinant proteins by providing a suspension-growing, serum-free adapted HEK293 cell line (293SF-3F6) that can be used to produce biologicals intended for animal or human therapeutic applications. Furthermore, it provides optimized feeding strategies and formulations of animal derived-free media and feed supplements to successfully operate fed-batch and perfusion cultures.

APPLICATIONS

- Large scale transient production of recombinant proteins and viral vectors and vaccines in suspension and under serum-free conditions.
- Generation of high producer and stable clones for large scale production of recombinant proteins and viral vectors
- Production of biopharmaceuticals using a cGMP master cell bank of a suspension-growing serum-free adapted HEK293 cell line.

CONCEPT

The complementing HEK293 cell line and its derivatives, the 293S cells, which have been adapted to suspension culture, are used for the production of recombinant proteins, including those requiring complex post-translational modifications for activity. Because these cells also sustain the replication of natural viruses or various recombinant viruses such as influenza or reovirus, they are useful for manufacturing of vaccines and oncolytic agents. They are also useful for the production of delivery vehicles for gene transfer, such as adenoviral, adeno-associated viral, lentiviral, and retroviral vectors. To simplify downstream processing as well as allow the production of recombinant proteins, vectors and vaccines in the quantities and purities required for human use, a broadly applicable stepwise approach was devised for the selection of animal cells capable of growth in serum-free conditions. This strategy was successfully used for the adaptation of suspension-growing HEK293S



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cells to commercially available serum-free media giving rise to the 293SF-3F6 cell line.

FEATURES AND BENEFITS

Useful approach to obtain serum-free viable cell lines and select chemically defined medium

The step-wise method allows animal cell lines that are viable in serum-free medium to be obtained and enables the selection of media formulations that best support growth and large scale production under chemically defined conditions. The method was successfully applied for the selection of a serum-free adapted clone (293SF-3F6) from a suspension-growing derivative of the human embryonic kidney cell line HEK293. Furthermore, the approach allowed selection and improvement of a preferred commercially available serum-free media for the production of recombinant proteins and viral vectors with 293SF-3F6 cells.

Efficient production of viral vectors and vaccines

The human embryonic kidney cell line 293SF-3F6 provides high cell growth rate in serum-free media and high-yield expression of various recombinant proteins and viral vectors and vaccines. Production has now been scaled-up to 500L scale.

Vectors	Application	Scale	References
Adenovirus	vaccines	500L	Kamen <i>et al.</i> , J. gene medicine, 2004
Gutless AdV	Muscular Dystrophy	3L	Dormond <i>et al.</i> , Biotechnol. Bioeng, 2009
AAV	Interferon	3L	Durocher <i>et al.</i> , VirMet, 2007
Retrovirus	Marker	3L, perfusion	Ghani <i>et al.</i> , Biotechnol. Bioeng, 2006
Lentivirus	Marker	3L, perfusion	Ansorge <i>et al.</i> JGM 2009.
Reovirus	Oncolytic	100L	Transfiguration <i>et al.</i> J.PBA, 2008
Influenza	Vaccine	3L	Le Ru <i>et al.</i> Vaccine, 2010

Availability of a Master Cell Bank (MCB) for cGMP production

In a further advancement, a cell clone of the 293SF-3F6 cell line was used to develop a MCB. Characterization and qualification of the cell line according to regulatory guidelines makes it suitable for the manufacturing of recombinant biopharmaceuticals intended for human use. This MCB can be used in the early stages of drug development as well as in the pre-clinical and clinical phases.

PROTECTION STATUS

Serum-free production of recombinant proteins and adenoviral vectors (NRC no. 10894).