

ADAPTATION OF VERO CELLS TO SUSPENSION CULTURE AND RABIES VIRUS PRODUCTION ON DIFFERENT SERUM FREE MEDIA

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Vero cells are nowadays widely used in the production of high quality vaccines for humans and animals. They are considered as one of the most productive and flexible continuous cell lines available for vaccine manufacturing. However, these cells are anchorage dependent, which greatly complicates upstream processing and process scale-up. Moreover, there is a recognized need to reduce costs of vaccine manufacturing in order to develop vaccines that are affordable worldwide. The use of cell lines adapted to suspension growth contributes to reach this objective.

The current work describes the adaptation of Vero cells to suspension culture in different serum free media according to multiple protocols. Then, the suspension adapted Vero cells (VeroS) were infected with rabies virus (strain LP-2061).

In addition to IPT-AFM (an in-house animal component free medium described in Rourou et al. 2009a; 2009b and 2014), five commercial formulations were analyzed for the establishment of serum free culture of VeroS. The cultures were performed in erlenmeyer flasks at 37°C, 5% CO₂.

The Cell doubling (CD) for VeroS adapted to IPT-AFM was $2,1 \pm 0,7$; the average specific growth rate (μ) reached $0,016 \pm 0,003 \text{ h}^{-1}$ and the maximum cell density (X_{max}) amounted to $2,16 \pm 0,9 \times 10^6$ cells/mL. Through adaptation, the cells behave differently in the different media. A comparative study was performed and IPT-AFM showed promising results.

Kinetics of rabies virus replication in VeroS cells grown in IPT_AFM showed that rabies virus was able to replicate in VeroS cells and to achieve a virus titer of 6×10^7 FFU/mL at day 3 post infection. These data show that the VeroS cell line can be considered as a suitable cell line for large scale rabies virus production.

Rourou S, van der Ark A, van der Velden T, Kallel H (2009a). Development of an animal-component free medium for Vero cells culture. *Biotechnol Prog.* 25(6):1752-61.

Rourou S, van der Ark A, Majoul S, Trabelsi K, van der Velden T, Kallel H (2009b). A novel animal-component-free medium for rabies virus production in Vero cells grown on Cytodex 1 microcarriers in a stirred bioreactor. *Appl Microbiol Biotechnol.* 85(1):53-63.

Rourou S., Ben Ayed Y., Trabelsi K., Majoul S. and Kallel H. (2014). An animal component free medium that promotes the growth of various animal cell lines for the production of viral vaccines. *Vaccine.* 32: 2767-2769.