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INCREASING OF PK15 BIOMASS FOR PCV VIRAL ANTIGEN PRODUCTION USING MODEL-BASED AND MEDIA OPTIMIZATION STRATEGIES THAT CONSIDER CELLULAR METABOLIC REQUIREMENTS

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Porcine circovirus associated disease (PCVD) is responsible for a significant economic loss in the livestock industry. A vaccine based on a viral antigen has been developed to prevent this disease, and it is produced industrially in the pig's kidney cell line PK15. However, both biomass and viral antigen production are limited in the current attachment culture bioprocess set-up.

The aim of this work is to improve PCVD vaccine production through the adaptation of PK15 cells to suspension culture, the introduction of changes in culture operation and the improvement of specific viral antigen productivity through media design.

The suspension culture of PK15 cells was achieved by means of a progressive cell adaptation process. Cells grown in suspension maintained a viability above 90% and a cell density equivalent to 0.7 times of that achieved in the original adherent culture.

Pseudo perfusion cultures were carried out using a 1 vvd rate, increasing the maximum cell density achieved to 8 times the base suspension culture. Feeding media was designed to decrease the perfusion rate to 0.1 vvd using the specific nutrient requirements of the cells determined experimentally. Results obtained at this higher density lower perfusion rate culture were comparable with those achieved at a 1 vvd rate in terms of biomass production.

A feeding strategy and feeding media composition was developed using a model-based platform CELIA (Cell culturE medIA optimization platform) that considers cell composition and metabolic requirements of the cells in culture. An increase of a 150% in biomass production was obtained using optimized feeding when compared to batch culture.

Viral antigen production data shows that even though total production increases significantly in all modes, specific productivity is lower when higher cell densities are achieved. Further research is required to optimize both the overall and specific productivity of the system.

Results show that it is possible to grow PK15 cells in suspension and to significantly increase the cell density obtained using perfusion culture and model-based media optimization tools that consider the cell's specific nutritional requirements. These findings will be validated in a semi-industrial setting model before transferring them to the industrial productive set-up.