COMBINING SINGLE-USE BIOREACTOR TECHNOLOGY AND TIPS METHOD TO MAKE IC/BEVS-BASED PRODUCTIONS MORE EFFICIENT

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Insect cells (ICs) in conjunction with the baculovirus-expression vector system (BEVS) are a suitable production system for the development and manufacturing of recombinant protein products such as virus-like particle vaccines. In order to speed up vaccine development and production, and to react more rapidly to pandemic scenarios, new strategies for IC/BEVS-based production technologies need to be developed and transferred. Among these is the implementation of single-use (SU) bioreactors, which have been proven as cost-effective (48 % less capital costs), ready-to-use systems without time-intensive cleaning and sterilization processes when compared with reusable bioreactors [1]. A further increase in process efficiency can be achieved by using the titerless infected-cell preservation and scale-up (TIPS) method. Here, the infection is directly performed with baculovirus-infected insect cells (BIICs), which makes laborious, time-consuming virus determinations and virus amplifications obsolete, while providing product titers and product activities comparable to the standard method, the classical infection of non-infected ICs [2, 3].

In our investigations we demonstrated the advantageous realization of the TIPS approach in a scalable, orbitally shaken single-use bioreactor, Adolf Kuhner's SB10-X, for the first time. Furthermore, we compared the results generated by producing the recombinant model protein secreted alkaline phosphatase (rSEAP) with those achieved in Sartorius Stedim’s stirred single-use bioreactor, the UniVessel SU 2L. All production processes ran for 6 days and were performed with Spodoptera frugiperda suspension cells (Sf-9) cultivated in Sf-900 III serum-free medium containing Pluronic F-68 and L-glutamine. Cell maintenance and seed inoculum production were carried out as described by Imseng et al. 2014 [4]. Samples were taken daily in order to determine cell growth (Cedex HiRes, Roche), substrate and metabolite concentrations (BioProfile 100plus, NOVA biomedical) as well as product formation [4]. When using the TIPS approach and working with a MOI of 0.01 pfu cell⁻¹ and a CCI of 2 x 10⁶ cells mL⁻¹, we achieved comparable rSEAP activities in the orbitally shaken and stirred single-use bioreactor. Saving four days in comparison with the standard method, we produced 158 U mL⁻¹ rSEAP in the OrbShake system operated with BIICs. These encouraging results represent the basis for scaling-up the TIPS approach to the orbitally shaken SB50-X in the future.

References: