Life Sciences and Facility Management

ICBT Institute of Chemistry and Biotechnology
ZHAW Zurich University of Applied Sciences
Campus Grüental, 8820 Wädenswil, Switzerland

Insect cell/ baculovirus expression vector system-based process developments

Summary

We are developing production processes based on the insect cell/ baculovirus expression vector system (IC/BEVS) platform for the manufacturing of recombinant protein products, including cell banking, cell expansion, recombinant baculovirus generation, virus titer determination, protein expression and relevant analysis. The production processes are performed in orbitally shaken, stirred and wave-mixed bioreactors from mL- up to 250 L scale (see Figure 1 and Imseng et al. 2014).

UniVessel SU | BIOSTAT RM | SB10-X

Figure 1: Single-use bioreactors for the production of recombinant proteins in insect cells.

Vision and activities

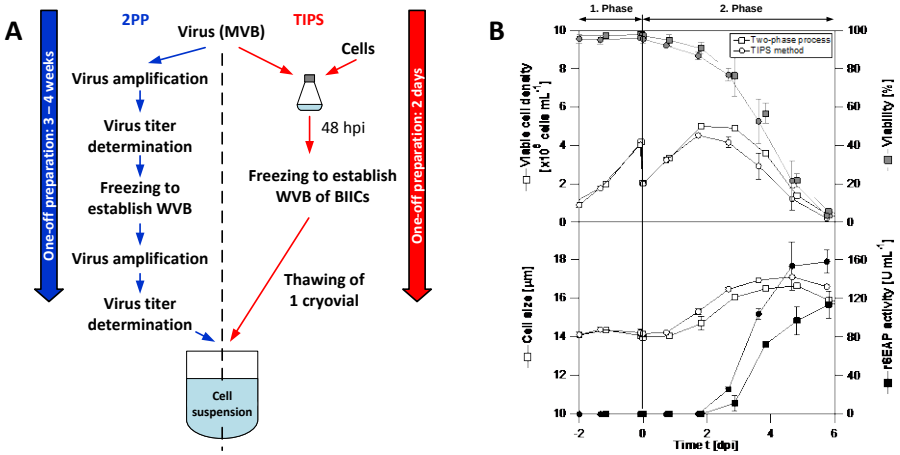

Figure 2: Comparison of the traditional two-phase process (2PP) - with the growth and production phase decoupled - with the TIPS method with regard to preparation time (A) and infection kinetics (B). (master virus bank (MVB), working virus bank (WVB), baculovirus-infected insect cell (BIIC), day post infection (dpi)). In this study, we worked with a *Spodoptera frugiperda* cell line (*Sf*-9), serum-free Sf900 III insect cell culture medium in 125 mL and 3 L shake flasks (Corning) and in the 10 L SB10-X (Kühner AG).

IC/BEVS-derived protein products have a great potential for a wide field of applications: gene therapy, vaccination, structure determination using crystallography, and screening of drug substances, as well as biological pest control. Our aim is to establish more efficient upstream processing technologies such as large volume cell banking procedures (Eibl et al. 2014), one-step cell expansion (Bögli et al. 2012), and titerless infected-cells preservation and scale-up (TIPS) methods (see Figure 2).

As shown in studies aimed at the production of the model protein recombinant secreted alkaline phosphatase (rSEAP) in our lab (Figures 2A and B), applying the TIPS method may be advantageous when compared to the traditional method. The preparation time (2 days instead of 3 – 4 weeks) was drastically reduced and up to 24 % higher protein activities were achieved (data shown for the SB10-X). In addition, the TIPS method eliminates the titering of virus stock supernatants and in general guarantees stable storage of highly concentrated recombinant baculoviruses enclosed in insect cells (baculovirus-infected insect cells (BIIC)).

Selected publications

- Single-use wave-mixed versus stirred bioreactors for insect-cell/BEVS-based protein expression at benchtop scale. N. Imseng et al., *Engineering in Life Sciences*, 2014
- Fast single-use VLP Vaccine productions based on insect cells and the baculovirus expression vector system: Influenza as case study. R. Eibl et al., *Advances in Biochemical Engineering/Biotechnology,* 2014
- Large-Scale, Insect-Cell–Based Vaccine Development. N. Bögli et al., *BioProcess International*, 2012
- A shaken disposable bioreactor system for controlled insect cell cultivations at milliliter-scale. C. Ries et al., *Engineering in Life Sciences*, 2010

Collaboration opportunities

In the past, we have successfully carried out projects in co-operation with Hoffmann-La Roche, Redbiotec and Andermatt Biocontrol in this field.

Research group leader contact details

Prof. Dr.-Ing. Regine Eibl
Group Leader for Cell Cultivation Techniques
Institute of Chemistry and Biotechnology
Zurich University of Applied Sciences (ZHAW)
Phone: +41 (0)58 934 5713
E-Mail: regine.eibl@zhaw.ch
Group Website: http://www.zhaw.ch/icbt/bioverfahrenstechnik

European cooperation contact

Dr. Agnes Zoller
Scientific Officer for European Research and Innovation
Institute of Chemistry and Biotechnology
Zurich University of Applied Sciences (ZHAW)
Phone: +41 (0)58 934 5295
E-Mail: agnes.zoller@zhaw.ch
Website: http://www.zhaw.ch/icbt/europeancooperations