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One Step ahead in Cell Cultivation – International Advanced Training Course at ZHAW Waedenswil

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Abstract: At ZHAW Waedenswil, students from all over the world meet to gain an insight into the laboratories and learn the latest processes in cell cultivation to produce drugs, vaccines and cosmetics. Under the guidance of Professor Regine Eibl, head of cell culture technology, they follow lectures, get to know how to handle insect, hamster and tobacco cells as part of a traineeship and visit industrial research labs – a unique opportunity to build up a network for the future.

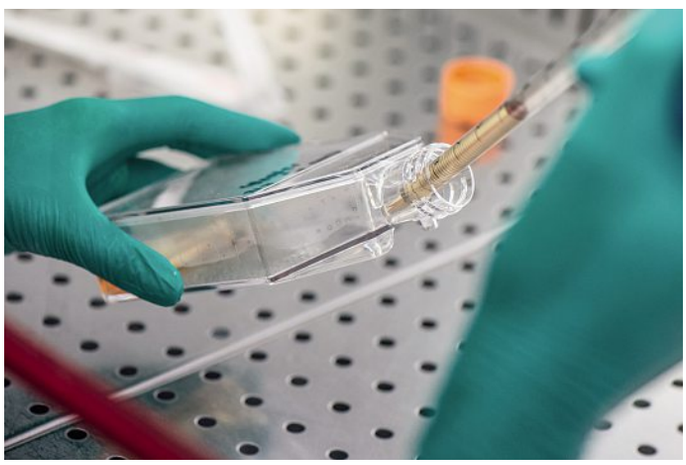
Keywords: Recombinant protein vaccines

Since the forties, egg-derived influenza vaccines have served to combat influenza infections. But to fight against unknown diseases and epidemics in the future we need faster, safer and high-yielding production methods. The solution is recombinant protein vaccines produced in insect cells.

Focus on Bio- and Cell Therapeutics

As an example, assume that company X has established a method for the increasingly popular recombinant VLP (virus-like particle) fabrication based on insect cells (sub clone HighFive™) and the BEVS (Baculovirus Expression Vector System). The initiators consider a fast, large-scale manufacturing process of a vaccine candidate for virus-like particle pandemic influenza A (H1N1) with obtainable single-use devices for upstream processes. What is the next step?

This is the topic of a case study within the *Advanced training course 2015* regarding '*Cell expansion and protein expression in standard and single-use bioreactors'* at the ZHAW Waedenswil from 11 to 28 August 2015, organised by Sören Werner, Deputy Head of Cell Cultivation Technique. "This crash course has been designed for Swiss and international students of biotechnology and related disciplines. The 24 participants learn how to cultivate animal and plant cells in standard and single-use bioreactors to realise bio-therapeutics such as antibodies or vaccines", explains Professor ***Regine Eibl***, Head of Cell Cultivation Technique. "It is also an opportunity for participants to get to know Switzerland and to create their own networks."



Subcultivation of CHO cells in T-flasks. Photo by ZHAW Wädenswil.

Students attend lectures given by highly-regarded scientists about cell cultivation techniques, deepen their theoretical background in practical lab work and develop their own biotechnological production process within a self-study. They benefit from the exchange of ideas with the Waedenswil scientists and the biotech experts they meet during their visits to facilities offered by ZHAW partners and sponsors of the event.

Nicotiana tabacum BY-2 suspension cells stained with Evans blue. The blue coloration indicates dead cells. Photo by ZHAW Wädenswil.

Biotech Issues in the Spotlight

The courses include, for example, the characterisation of mammalian cells, metabolism and culture medium, a comparison of reusable and single-use bioreactors, and also explain how we can rapidly scale-up animal cell-based processes, and present CFD (Computational Fluid Dynamics) as an important tool for characterising cell culture bioreactors and developing processes. Emphasis is also placed on specialities of micro-carrier-based processes and troubleshooting.

In small groups the students experience practical on-the-job training in issues such as the mass propagation of insect cells in a small-scale single-use bioreactor, Immunoglobulin G (IgG) production with plant cells in orbitally shaken and wave-mixed bag bioreactors, and the cultivation of BHK (Baby Hamster Kidney) cells on micro-carriers in T-flasks.

The work on current subjects such as the plant suspension cell-based IgG production, the mass propagation of terpenoid expressing hairy roots or the expansion of mesenchymal stem cells in single-use bioreactors is ideal for the self-study process.

Hairy root cultures – a special tissue which exhibits superior genetic stability. Photo by ZHAW Wädenswil.

Standard stirred bioreactor at laboratory scale, prepared for the cultivation of mammalian cells, running a sterility test. Photo by ZHAW Wädenswil.

Highly specialised experts operate and lead the workshops. The first workshop refers to 'Standard and single-use cell culture bioreactors' and brings together Sartorius Stedim Biotech, GE Healthcare, Pall Corporation, INFORS HT, Bioengineering AG, the biotech company Eppendorf and Alvotech. The second explains 'Chemically defined minimal culture media' and is led by Dr. ***Ferruccio Messi***, President and CEO of Cell Culture Technologies Lab Ltd.

Why Do Students Sacrifice their Holidays?

In order to achieve optimum learning success, participants have to meet certain requirements: they should be trained in aseptic working techniques, and have a basic knowledge in biotechnology and proficiency in English to the level of a First Certificate in English as a minimum. Students from all over Europe benefit from the professional exchange in an international atmosphere and – although the course takes place in the summer holiday period – they unanimously agree that the time spent here is definitely worth it.

Yorick van Eimeren studies at the HAN University of Applied Sciences in the Netherlands. So far, he has concentrated on the cultivation of bacteria and yeasts. "In Waedenswil, I would like to gain a deeper insight into different bioprocesses for the production of pharmaceutical active substances, in particular upstreaming and use of plant and animal cells", explains Yorick. For the future he is especially interested in the development of

Student Yorick van Eimeren from the Netherlands wants to extend his knowledge on different bioprocesses for the production of pharmaceutical active substances. Photo by Elsbeth Heinzelmann.

therapeutic proteins and generally in medical compounds with high added value.

Irina Volkova has come a long way: she is from Ya. R. Kovalenko All Russian State Research Institute of Experimental Veterinary Medicine in Moscow. Her domain is the 3D microcarrier-based cultivation of stem cells primarily in conventional bioreactors. "I would like to learn about the whole spectrum of human, plant and animal cells such as mammalian cells and insect cells", reveals Irina. "Furthermore, I am interested in bioprocesses for the expansion and differentiation of cells of animal and human origin. Fascinating aspects include the screening of cell lines, process and parameter scouting and scale-up." Waedenswil is her second stay abroad. Her first was in Sweden, where she got a glimpse behind the scenes of the production of natural food flavourings for foodstuffs such as sauces, crisps and meat products." But concerning technical assistance, the infrastructure and laboratory equipment in the ZHAW course is definitely exceeding my expectations", concludes Irina.

Strong ties with student exchanges exist between the ZHAW and the Anhalt University of Applied Sciences in Köthen, where Professor Regine Eibl gained her degree in biotechnology. It is therefore not surprising that five students – men and women – were motivated by their professors to attend the course. One of them is Bettina Preylowski. As the cell culture technology at ZHAW Waedenswil is reputed to be some of the best on an international level, she wants to learn as much as possible about

this subject. "Here I found a good mixture of lectures, practical work using the latest laboratory equipment, workshops with specialists in the domain and biotech company tours. You won't be bored", she reports with a smile. "Moreover, there are always opportunities to exchange ideas with the ZHAW researchers or experts from the industry."

Tailored to the Needs of Industry

The Advanced Training Course corresponds to the industry's increasing need for a qualified specialist workforce, a fact confirmed by Dr. ***Kurt Leimbacher***, President of Swiss Process and Chemical Engineers (SGVC). "We are following the promotion of process and chemical engineering in two ways: by supporting young talent – in particular women – and by continuing training with events about topical themes."

INFORS HT, near Basel, a specialist in bioreactors, incubation shakers and bioprocess control software, enjoys an especially close relationship with ZHAW Waedenswil. "We also require skilled professionals, primarily to fill key positions at INFORS HT", explains ***Daniel Egger***, Director of Marketing and himself a former student of ZHAW. "We cultivate an intensive interchange with the Waedenswil researchers, regarding state-of-the-art equipment and software, and we frequently cooperate in projects supported by CTI, the Commission for Technology and Innovation."

The effort that goes into organising the course is considerable, but it pays off: "Our courses typically fill up very quickly, probably because the professional skills learned here are exactly the competences that the industry requires. This particularly applies to the use of and efficient dealing with single-use equipment where market researchers predict significantly higher rates of growth in the future", concludes Regine Eibl, internationally renowned expert in the domain of disposable bioreactors. "That's why we intend to strengthen our partnership both in Switzerland and abroad for an enhanced course programme in single-use technology." The relevant concept will be presented at 'Biotech 2016', which will be held in Waedenswil from 5 to 7 September 2016.

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Regine Eibl and team