



Master in Life Sciences

A cooperation between
BFH, FHNW, HES-SO, ZFH

Module	Big Active Molecules
Code	MSLS_V3_2
Degree Programme	Master of Science in Life Sciences (MSLS)
ECTS Credits	4
Workload	Total 120 h: Contact 60 h; Self-study 60 h
Module Coordinator	<p>Name Dr. Sabina Gerber</p> <p>Phone +41 (0)58 934 54 28</p> <p>Email sabina.gerber@zhaw.ch</p> <p>Address ZHAW Zurich University of Applied Sciences Life Sciences and Facility Management Campus Reidbach PO Box CH-8820 Wädenswil</p>
Lecturers	<ul style="list-style-type: none"> • Dr. Sabina Gerber, Prof. Dr. Martin Sievers
Entry Requirements	<ul style="list-style-type: none"> • Solid knowledge of biochemistry and analytical chemistry • Solid knowledge of protein structure and function • Basic knowledge of protein purification • Basic knowledge in molecular biology • Basic knowledge in cell culture technology
Learning Outcomes and Competences	<p>After completing the module students will be able to</p> <ul style="list-style-type: none"> • understand the use of recombinant proteins as therapeutics • understand the structure and function of monoclonal antibodies • use of bioinformatic tools • understand and be able to apply methods of downstream processing • understand and be able to apply in-process control and quality control methods • understand and be able to apply methods of molecular biology and cell culture technology
Module Content	<p>Topics of the module are Big Active Molecules - in particular proteins - in contrast to Small Active Molecules, organic molecules of low molecular mass. The main focus will be on recombinant antibodies which are the most important molecules in pipeline of the pharmaceutical industry. The structure and function of antibodies and the amazing way evolution has created a system to produce billions of different antibodies in an organism by genetic recombination will be discussed. The basis for the specific antigen recognition of these billions of antibodies by the three-dimensional arrangement of the hypervariable CDR regions will be explained. The understanding of state-of-the-art technologies to select monoclonal antibodies (mAb)</p>

	<p>as therapeutic molecules such as phage display and transgenic mouse strains expressing human antibodies will be followed by the introduction of the diverse formats of engineered antigen binders. These encompass not only antibodies and the different antibody fragments but also protein scaffolds e.g. DARPin. The biological activity of most proteins depends on posttranslational modifications. The influence of glycosylation on the activity of erythropoietin and of mAb will be discussed together with the methods used for analysis.</p> <p>Two practical courses “Downstream processing and analytics” and the “Molecular biology and mAb expression” will be offered and students will be distributed between the two courses.</p> <p>In the practical course “Downstream processing and analytics” the downstream process of a mAb as used in pharmaceutical industry is performed in small scale. The different process steps will be monitored by in-process controls. The final product, corresponding to the active pharmaceutical ingredient, will be analyzed with the same methods as in the pharmaceutical quality control of a drug substance (analytics of target molecule and impurities such as host cell proteins, host cell DNA etc.).</p> <p>In the practical course “Molecular biology and mAb expression” the main focus lies on the development of a CHO cell line expressing a monoclonal antibody. Total RNA from a hybridoma cell line expressing a monoclonal antibody is prepared. The VL and VH fragments are amplified by using reverse transcription PCR (RT-PCR) with family-specific primer pairs. The DNA sequences of the PCR products are determined. A cloning strategy is developed to obtain full-length antibodies. The amplified VL fragment is cloned into the vector pFUSE2-CLlg-hK (InvivoGen). The vector expresses the constant region of the human kappa light chain and contains the signal sequence from the interleukin-2 gene. For cloning of the VH fragment the vector pFUSE-CHlg-hG1 (InvivoGen) is used. The vector contains the CH1, CH2, CH3 sequences of the human IgG1 heavy chain and the signal sequence from the interleukin-2 gene. The cloned constructs (both vector with ligated VL and VH fragments) are transfected simultaneously in CHO cells. Selection of the CHO cells is based on the expression of blasticidin and zeocin resistance genes located on the plasmids. The CHO cell line is assayed by ELISA for monoclonal antibody expression.</p>
Teaching / Learning Methods	<ul style="list-style-type: none"> • Lectures with exercises • To supplement the contents of the lecture, reading of relevant scientific literature in self-study mode and discussion thereof • Practical course with lectures allowing close integration of practical and theoretical aspects • Troubleshooting and critical discussion of results • Self-dependent practical project including planning, performance and analysis of results • Presentation of results from project
Assessment of Learning Outcome	<ul style="list-style-type: none"> • Written examination (50 %, Recombinant proteins as therapeutics) • Written report and oral presentation or poster (50 %, “Downstream processing and analytics” or “Molecular biology and mAb expression”)
Bibliography	Selected original papers and book-chapters
Language	German / English
Comments	
Last Update	26.09.2021