Module	**Biodesign: Ways to Active Pharmaceutical Ingredients**
Code	MSLS_V2_1
Degree Programme	Master of Science in Life Sciences (MSLS)
ECTS Credits	5
Workload	150 h: Contact 60 h; Self-study 90 h
Module Coordinator	**Name** Prof. Dr. Jack Rohrer **Phone** +41 (0)58 934 57 17 **Email** jack.rohrer@zhaw.ch **Address** ZHAW Zürcher Hochschule für Angewandte Wissenschaften Life Sciences and Facility Management Campus Reidbach Postfach CH-8820 Wädenswil
Lecturers	• Dr. Steffi Lehmann • Dr. Lukas Neutsch • Prof. Dr. Jack Rohrer • Prof. Dr. Martin Sievers
Entry Requirements	The particular Master's module builds on a standard Bachelor's level courses which convey basic knowledge in the following fields (see also textbooks given in brackets): • Biochemistry (Berg J.M., Tymoczko J.L, and Stryer L., 2012. Biochemistry: International Edition. 7th Ed., W.H.Freeman & Co Ltd) • Biotechnology (Renneberg R., 2007. Biotechnology for Beginners. Academic Press) • Microbiology (Fuchs G. and H.-G. Schlegel., Allgemeine Mikrobiologie. 8th Ed., Georg Thieme Verlag) • Molecular biology • Pharmacology (Hein L., Mohr K., and Lüllmann H., 2008. Taschenatlas der Pharmakologie, Georg Thieme Verlag)
Learning Outcomes and Competences	After completing the module students will be able to • evaluate the therapeutic and the market potential of biopharmaceuticals based on pharmacological, pharmaeconomical and pharmacovigilance data • explain the principle methods and strategies of the drug discovery process and evaluate the advantages and disadvantages of different technologies • select for each DNA sequence a suitable expression system and to adapt a DNA-sequence allowing an optimal protein production in terms of productivity, quality, safety and cost-effectiveness

	• understand how to modify expression strains (yeasts, insect cells) to achieve a targeted glycosylation pattern • apply acquired theoretical knowledge of all standard techniques to construct a system for production of recombinant proteins and enzymes, including cellular or secreted proteins, the anchoring of proteins on cellular surfaces, and the humanisation of monoclonal antibodies
Module Content	As most lifestyle diseases are still treated symptomatically and no effective therapies exist for other common diseases, the search for new drugs is on-going. Candidate molecules and lead structures can be found in the biosphere, redesigned by computing methods or adapted to mimic known physiologically active molecules. Often these molecules are of protein nature and can be produced by recombinant DNA technology. Therefore, there is an increasing demand of new and optimised expression systems using different production organisms. Afterwards a transfer to biotechnological production processes is required. The following topics will be covered: • definition and classification of biopharmaceuticals, pharmacology of biopharmaceuticals • biopharmaceutical sales, market analysis and global changes in the health care sector • pharmacology of novel biopharmaceuticals and pharmacovigilance • strategies in drug discovery: combinatory chemistry, (ultra) high-throughput-screening, omics-technologies, computer-aided drug design • use and evaluation of different production systems to find new drugs • construction of vectors, adaptation of codon usage for the expression host, optimisation of transcription and translation as well as fusion of gene sequences • design of expression systems for glycosylated proteins, proteins with disulfide bonds, secreted proteins or membrane proteins • theoretical background for the production of humanised antibodies • strategies for the design of assays to compare expression hosts • principles of high-throughput clone/library screening methods • decision criteria: requirements of the end-product, manufacturing procedure and costs • basics of synthetic biology • best practice for screening of production clones • adaption of production strains used for biotechnological manufacture in industrial scale to maximise productivity (titre, yield) or product quality
Teaching / Learning Methods	• contact lessons • group work • case studies • literature and database search • computer-aided design
Assessment of Learning Outcome	• Written exam 60% • Report 33% • Poster 7%
Bibliography	• Blume A., Ghaderi D., Liebich V., Hinderlich S., Donner P., Reutter W., Lucka L. 2004. UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase, functionally expressed in and purified from Escherichia coli, yeast, and insect cells. Protein Expr. Purif. 35: 387-396.

	• Bork K., Reutter W., Weidemann W., Horstkorte R. 2007. Enhanced sialylation of EPO by overexpression of UDP-GlcNAc 2-epimerase/ManAc kinase containing a sialuria mutation in CHO cells. FEBS Lett. 581:4195-4198. • Cobert B. L. 2006. Manual of Drug Safety and Pharmacovigilance. Jones & Bartlett Publishers • Dübel S. (Ed.). 2010. Handbook of Therapeutic Antibodies: Technologies, Emerging Developments and Approved Therapeutics. Wiley-Blackwell • Hartner, F.S., C. Ruth, D. Langenegger , P. Hyka, G. P. Lin-Cereghino, J. Lin-Cereghino, K. Kovar, J. M. Cregg, and A. Glieder. 2007. Engineered Pichia pastoris AOX1-based promoter libraries for fine-tuning gene expression. Nucleic Acids Res. 36: e76 • Hemmasi S., Czulkies B.A., Schorch B., Veit A., Aktories K., Papatheodorou P. 2015. Interaction of the Clostridium difficile binary toxin CDT and its host cell receptor, lipolysis-stimulated lipoprotein receptor (LSR). J. Biol. Chem. 29:14031-1444. doi: 10.1074/jbc.M115.650523. • Hillisch A., and R. Hilgenfeld. 2003. Modern Methods in Drug Discovery, Birkhäuser Verlag, Basel • Hyka, P., T. Zullig, C. Ruth, V. Looser, C. Meier, J. Klein, K. Melzoch, H. P. Meyer, A. Glieder, and K. Kovar. 2010. Combined use of fluorescent dyes and flow cytometry to quantify the physiological state of Pichia pastoris during the production of heterologous proteins in high-cell-density fed-batch cultures. Appl. Environ. Microbiol. 76:4486-96. • Gellissen, G. (Ed.). 2005. Production of Recombinant Proteins. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany. ISBN 3-527-31036-3 • Knablein J.2005. Modern Biopharmaceuticals, Volumes 1 to 4, Wiley • Vogel H. G. 2007.Drug Discovery and Evaluation: Pharmacological Assays, Springer Berlin; Auflage: 3 • Kovárová - Kovar K., S. Gehlen, A. Kunze, Th. Keller, R. von Däniken, M. Kolb, and A.P.G.M. van Loon. 2000. Application of model -predictive control based on artificial neural networks to optimize the fed-batch fermentation process for riboflavin production. J. Biotechnol. 79: 39-52. • Lu J., Wei D., Wang Y., Wang G. 2009. High-level expression and single-step purification of recombinant Bacillus anthracis protective antigen from Escherichia coli. Biotechnol. Appl. Biochem. 52: 107-112. • Rascati K. 2008. Essentials of Pharmacoeconomics: An Introduction. Lippincott Williams & Wilkins • Sievers M., Uermösi C., Fehlmann M., Krieger S. 2003. Cloning, sequence analysis and expression of the F1F0-ATPase beta-subunit from wine lactic acid bacteria Syst. Appl. Microbiol. 26: 350-356 • Swiech K., Picanço-Castro V., Covas DT. 2012. Human cells: new platform for recombinant therapeutic protein production. Protein Expr. Purif. 84: 147-153. • Xiong H., Li S., Yang Z., Burgess R.R., Dynan W.S. 2009. E. coli expression of a soluble, active single-chain antibody variable fragment containing a nuclear localization signal. Protein Expr. Purif. 66: 172-180.
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Comments	
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