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NGS analysis of miRNA expression patterns concerning therapeutic protein production and protein glycosylation in recombinant CHO DG44 cells

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Mature miRNAs are 19-25 bp long RNA duplexes, which are associated with RISC (RNA induced silencing complex) and bind to mRNAs leading to translational expression. It has been shown, that miRNAs also play a role in regulation of productivity and cell growth in CHO cells. This work investigates the role of miRNA in recombinant protein production in CHO DG44 cells including a variety of different products with production-relevant final product concentrations (up to 8 g/l in fed-batch mode). Additionally, the influence of miRNA on the glycosylation pattern of the recombinant protein is investigated. In detail, 24 clonal cell lines expressing four different therapeutic proteins are selected based on final product concentrations and glycosylation patterns. These clones were cultivated in an ambr® 15 system in fed-batch mode collecting process and glycosylation data. Cell samples are used for NGS of small RNA on the Illumina NextSeq System. Between 150 and 200 predicted small RNAs were found in each cell line. Of these, 10 to 20% are putative novel and could not be found in miRBase 2, Rfam 13.0 or RNAdb 2.0. Overall, 394 distinct miRNAs could be identified. Differential analysis revealed that there is great variety between therapeutic protein groups, as differentially expressed miRNAs was only recurred in maximum two of these groups. In a follow-up study, 5 to 10 differentially expressed miRNAs of each product group will be tested for their effects on therapeutic protein production and glycosylation in CHO DG44 cells.

Biography

Ann Cathrin Leroux studied BSc in Medical Biotechnology at Univesity of Rostock, Germany and Pharmaceutical Biotechnology at Ulm University, Germany. She is currently working on her PhD at Sartorius Stedim Gellca GmbH and Ulm University. She has completed Master studies at Ulm University and University of Applied Sciences Biberach, Germany. Her master thesis research field includes: Influence of promoters on the productivity of CHO DG44 cells, performed at Sartorius Stedim Cellca GmbH. She has done her Bachelor studies at University of Rostock, Germany.

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