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Production of antibody fragments with plasmid-based and genome integrated T7 *E. coli* expression systems: Evaluation of systems performance in microtiter fed-batch like cultivations

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Although *E. coli* is the most prominent bacterial production host for recombinant proteins, some proteins with high economic potential can still hardly be produced at remunerative levels. We selected four different Fabs (Fragment, antigen binding) (BIBH1, BIWA4, CIMZIA and FabX) with identical constant domains representing such challenging proteins. Fab yield can be affected by miss-folding, aggregation or unbalanced expression, translation and translocation levels of sub-units, making it still challenging to efficiently design expression systems and production processes. For translocation to the periplasm a post-translational (ompA) and a co-translational (dsbA) leader sequence were used. *E. coli* BL21(DE3) and *E. coli* HMS174(DE3) were transformed either via pET vectors or genome integration. The resulting 32 clones, were cultivated under fed-batch like conditions in the BioLector. Cell growth was not affected by leader/Fab combinations but yield of correctly folded Fab ranged from 0 to 12.5 mg/g CDM. Higher expression rates caused higher amounts of free light chain and K12 strain reached higher yields. Except of CIMZIA with the dsbA leader, genome integrated versions showed higher Fab yields, reduced levels of free light chain and basal expression than plasmid-based systems. Independent from used expression system, highest yields were obtained with CIMZIA followed by BIWA4, BIBH1 and FabX. Leader sequence cleavage-efficiency for DsbA was significantly lower than for OmpA, both showed lowest with CIMZIA. Summarizing, we showed that the selected set of host/gene dosage/leader/Fab combinations resulted in a broad range of variation in terms of Fab yields and processing and will be studied detailed in bench-scale fermentations.

Biography

Monika Cserjan has completed her PhD at the University of Natural Resources and Life Sciences, Vienna in 1998. She is Senior Scientist in the Christian Doppler Laboratory for production of next-level biopharmaceuticals in *E. coli* at the Department of Biotechnology (Fermentation Technology Group), Vienna and Project Leader at the Austrian Centre of Industrial Biotechnology (ACIB).

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