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Description:

Approx. 60-70% of all relevant pharmaceutical proteins are produced via **transfection** of the corresponding genes into mammalian cells (Fig. 1). Establishing a stable and efficient cell line can take up to 12 months. More rapid expression of small amounts of proteins (e.g. for evaluation purposes) can be achieved by **transient expression** (i.e. without incorporation of the DNA into the cell's genome). Conventionally, viral vectors are utilized to deliver genetic material into the cells. Viral vectors are very efficient; however, **non-viral vectors** are more desirable in order to reduce the risk of producing toxic byproducts and to avoid viral replication. Examples for non-viral vectors are calcium phosphate, modified PEI or peptides. However, their efficiency is considerably lower.

Our project aims at obtaining **detailed quantitative knowledge** about transient gene expression of *HEK293* cells and the subsequent development of a model-driven **optimization strategy** for **industrial protein production** processes, yielding high product concentration with high reproducibility.

In a DFG cooperation project, our group focuses on the development of analytic methods for quantification and a mathematical model for kinetic analysis of the intracellular and epigenetic processes during transient gene expression. The influence of cell growth, metabolism and apoptosis will be taken into account. In collaboration with the group of Dr. Wirth (Helmholtz Centre for Infection Research, Braunschweig), a **new generation** of vectors is investigated. Based on the modeling results, bottlenecks during gene expression will be identified and eliminated.

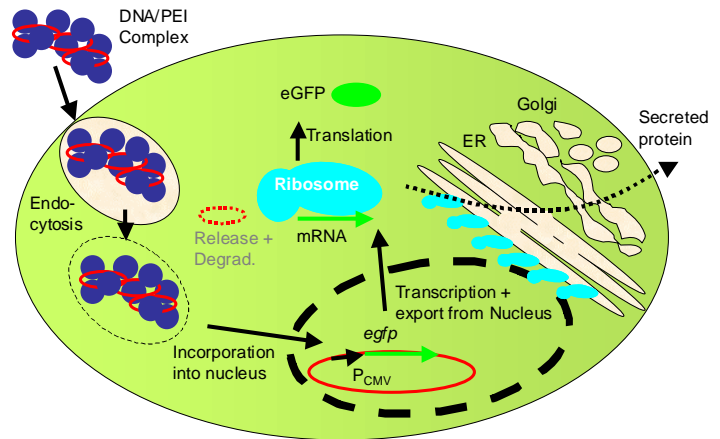


Fig.1: Scheme of transfection and transient expression. Genetic material is introduced into the cell using either nonviral (shown) or viral vectors. The DNA is incorporated into the nucleus. Finally, pharmaceutical proteins (or reporter proteins) can be expressed via transcription, mRNA export and translation and secreted.

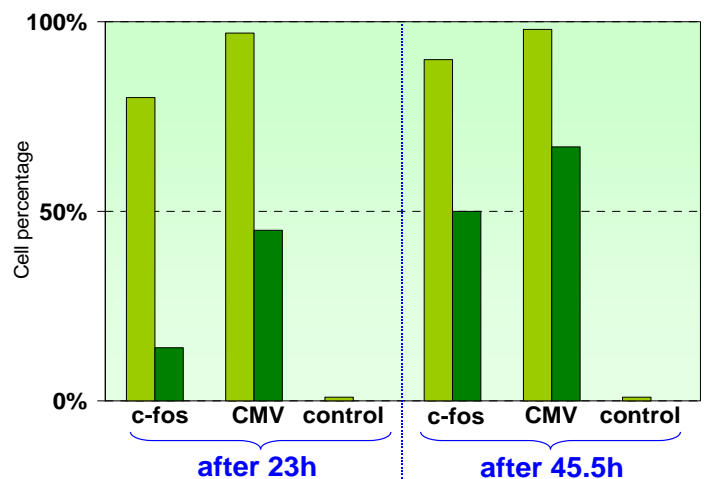


Fig. 2: Example of the transfection kinetics using different promoters (c-fos and CMV). Light green: Transfected cells; Dark green: good producers.

References

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- Bi, JX, Buhr, P, Zeng, AP, and Wirth, M (2003). **Human c-fos promoter mediates high-level, inducible expression in various mammalian cell lines**. *Biotechnol. Bioeng.*, 81(7):848 – 854.

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