



Master Thesis Project protein expression: Development of super-CHO

Start: January 2023, flexible duration but not less than 20 weeks

Suitable background for applicant: Major in molecular biology or biotechnology and experience from cell culture.

Supervisors: Daniel Ivansson and Ann Lövgren, Cytiva R&D, Björkgatan 30, Uppsala

Background

- *Antibody expression in recombinant stable cell lines depends on several factors such as gene dosage, site of integration, promoter, and other control elements, but also on how well-adapted the host cells are for producing and growing under the selected conditions. Such adaptation depends to a large extent on epigenetic factors. During adaptation, the cell is reprogrammed, and expression of genes can be both up and down regulated. Events that are stressful to the cells, such as exposure to certain chemicals and single cell cloning have been shown to cause changes to DNA methylation pattern and mRNA expression profile suggesting that the cells have been re-programmed. Epigenetic reprogramming can work in different directions, so that stably transfected cell lines can either lose or gain in productivity of the expressed protein. In this context, it is today not known to what extent epigenetic programming is maintained when cells are subjected to repeated stress such as repeated subcloning.*

What you will do:

- *Cytiva has developed a CHO Cell Platform enabling Site Directed Integration (SDI) of genetic payloads into a defined genomic location.*
- *In this exam work project, you will use the SDI platform in a proof-of-concept study around adaptation and epigenetics in stable cell lines.*
- *The project will utilize stable cell lines derived from our site-directed integration platform. The cell lines are isogenic but with varying productivity so that it can be investigated if the productivity phenotype is maintained or altered under different conditions such as recombination events and single cell cloning.*
- *The overall aim of the project is to investigate if a superior host cell line can be obtained by adaptation and selection due to epigenetic changes. In addition, different regulatory elements will be investigated.*
- *Independently solve problems of "trouble shooting character" in project work.*
- *Maintain laboratory notebooks in accordance with company policy and legal requirements.*
- *Present scientific and technical results internally, through oral and written communication in Swedish and English.*

Who you are?

- *To succeed in this position, you need to be result-oriented, flexible, and creative with a strong collaborative attitude*
- *We are looking for someone with the drive and capability to initiate, individually or in co-operation with others, plan, perform, analyse, document and present results to progress the project forward.*

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Send your application to ann.lovgren@cytiva.com or daniel.ivansson@cytiva.com