Master Thesis Project optimization of clone selection platform for production of recombinant proteins with biotechnological applications

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: Srdja Drakulic and Thomas Falkman, Cytiva R&D, Björkgatan 30, Uppsala
srdja.drakulic@cytiva.com thomas.falkman@cytiva.com

Be part of something altogether life-changing

Working at Cytiva in the Life Sciences industry means being at the forefront of providing new solutions to transform human health. Our incredible customers undertake life-saving activities ranging from fundamental biological research to developing innovative vaccines, new medicines, and cell and gene therapies.

At Cytiva you will be able to continuously improve yourself and us – working on challenges that truly matter with people that care for each other, our customers, and their patients. With associates across 40 countries, Cytiva is a place where every day is a learning opportunity – so you can grow your career and expand your skills in the long term.

Cytiva is proud to work alongside a community of nine fellow Danaher Life Sciences companies. Together, we're pioneering the future of science and medicine, developing products that enable researchers in the fight to save lives.

Background
Drugs represent major "weapon" in a fight against diseases and for improving human health. Based on their production, drugs could be assigned to one of two groups:

- **Traditional pharmaceutical drugs** - small molecules, produced by chemical processes.
- **Biologics** - generated by living cells or in biological process.

The latter are more complex and highly dependent on production process and starting material, due to which there is a significant discrepancy in the number of critical tests necessary to control production of these two groups of drugs: 40-50 for small molecules and over 250 for biologics. This drastically increase production costs and approval procedures, being also a major cause for huge difference in number of therapies based on the use of the two types of drugs (i.e., 885 vs 133 in the period from 1982 to 2017). The biggest share of the biologic's market today is held by monoclonal antibodies (mAbs), with a Chinese Hamster Ovary cell (CHO) employed as a major working horse.
A typical production process consists of number of steps that could be roughly grouped into:

- **Upstream processing (USP)** - covers all the steps from the thawing of a cell that produces product of interest, amplification, to cell culturing at the large-scale, using bioreactors.
- **Midstream processing (MSP)** – or a primary product recovery, encompasses, cell lysis (if necessary), separation of product from cells and/or cell debris.
- **Downstream processing (DSP)** – comprised of all purification steps.

The cell line development and upstream process optimization represent major bottlenecks of the entire pathway from the discovery of a molecule with potential therapeutic/biotechnological application to its cost efficient (commercial) manufacturing, which on the other hand should generate a molecule of interest at superior yields, with defined quality and in highly reproducible manner. Production of therapeutic proteins in general, and antibodies in particular, is determined by a number of factors: gene dosage, site of integration, type of cis-regulatory elements, metabolic activity of a host cell, type of production process and the capacity of host cell(s) to sustain different stressors. Therefore, identification of the "best" clone (reaching highest specific and volumetric productivities) represents if not a key but one of key steps towards manufacturing of a protein of interest.

What you will do:

- The project will utilize stable cell lines derived from our CHO platform, based both on Random and Site Directed Integration (RI and SDI, respectively).
- Perform set of experiments that will allow to establish robust platform for clone selection step: i.e., determine the adequate moment for a feed onset; and test different feed regimes; You will be able to learn design of experiment (DoE) approach, how to analyse and trace basic metabolic pathways and cell culture kinetics, as well as how to access product quality attributes (i.e. titre, aggregates, charged variants).
- 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

- In order 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.

When you join us, you'll also be joining Danaher's global organization, where 68,000 people wake up every day determined to help our customers win. As an associate, you'll try new things, work hard, and advance your skills with guidance from dedicated leaders, all with the support of powerful Danaher Business System tools and the stability of a tested organization.

Danaher is committed to a diverse and inclusive culture where everyone feels they belong, and all voices are heard. We believe in our associates and the unique perspectives they bring to every challenge, which is why we'll empower you to push the boundaries of what's possible.

If you've ever wondered what's within you, there's no better time to find out.

Danaher Corporation and all Danaher Companies are equal opportunity employers that evaluate qualified applicants without regard to race, colour, national origin, religion, sex, age, marital status, disability, veteran status, sexual orientation, gender identity, or other characteristics protected by law. The "EEO is the Law" poster is available here.