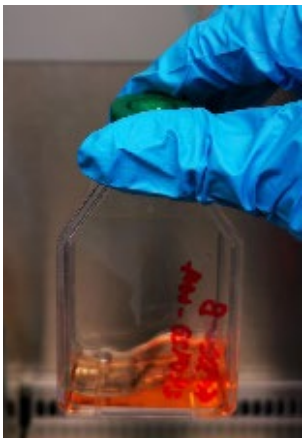
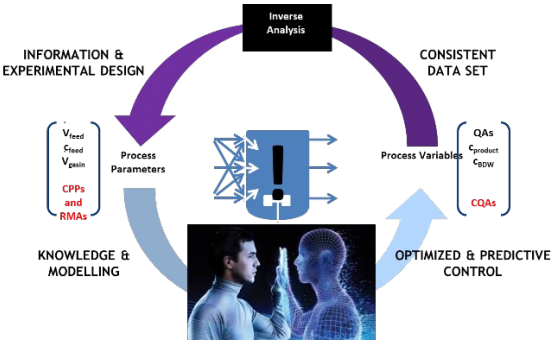
DIGITAL TWIN-BASED BIOPROCESS DEVELOPMENT FOR CELL AND GENE THERAPY

Application of sound science methodology for technologizing NK cells processes:





From development *via digital twin methods* *to predictive ATMP processing*

Supervisory Team[1]

Primary Supervisor:

Univ.-Prof. Dr. Christoph Herwig; Biochemical Engineering; Institute of Chemical, Environmental and Bioscience Engineering (ICEBE), TU Wien

TU Wien project partners:

Assoc. Prof. Dr. Astrid Mach-Aigner; Biochemical Technology; Institute of Chemical, Environmental and Bioscience Engineering (ICEBE), TU Wien

Univ.-Prof. Dr. Robert Mach; Biochemical Technology; Institute of Chemical, Environmental and Bioscience Engineering (ICEBE), TU Wien

Univ.-Prof. Dr. Radu Grosu; Institute of Computer Engineering; TU Wien

Assoc. Prof. Dr. Clemens Heitzinger; Institute of Analysis and Scientific Computing; TU Wien

External academic partners:

Reinhard Fischer; KIT, Germany

External industry partners:

Jens Tränkle; Bayer AG, Germany

Volker Huppert, Glycostem, The Netherlands

[1] The Early Stage Researchers (ESRs) will be accompanied during their thesis by an individual "Thesis Advisory Committee" (TAC), which will guide the ESR through the graduate studies. The TAC will consist of the thesis primary supervisor, and two additional members of the Supervisory Team selected by the ESR.

Project Description

Advanced Therapy Medicinal Products (ATMPs) are perceived as key enablers for personalized medicine. For example, proliferated Natural Killer (NK) cells can be used for cancer treatment. However, NK cell attributes differ from donor to donor, leading to large process variations and finally to mismatch in product quality. Hence, next generation therapy processes have to be technologized. However, the cellular complexity of metabolism, differentiation and function is too large to reply on pure measurements only. Our hypothesis is that a digital twin based approach can yield efficiently to the desired robust and stable expansion process.

Therefore, this PhD project focusses on the development of kinetic and metabolic process models to describe and steer NK cell expansion to optimal and reproducible Critical Quality Attributes (CQA). Based on real-time implementation as digital twin, critical process events can be predicted to achieve a robust expansion step and constant CQAs across multiple donors. This PhD therefore is a translational opportunity to use our reputed tools of PAT, experimental design and digital twins on NK-ATMP processes and allow for providing platform knowledge for next generation biopharmaceuticals.

Key Goals and Tasks

The primary aim of this PhD thesis is to develop and deploy digital twins to technologize and enable robust ATMP processes, using NK cells as a model system.

Tasks:

- Learn NK cell cultivation techniques and analytics as established in our labs
- Gather process understanding by relating CQAs to raw material attributes and process parameters using multivariate experimental designs
- Convert the gathered process understanding in hybrid models using good modelling practice workflows
- Set up the Process Analytical Technology (PAT) strategy and deploy the model in real time as digital twin. The real time environment is well established in our labs.
- Verify the robustness of the digital twin predictions, refine the hybrid model by using different starting materials and process conditions
- Publish high impact publications in this novel and emerging field of enabling affordable drugs for the world

Project-specific Requirements

- Completed master studies in Bioprocess Technology, Biotechnology, Electrical Engineering, Chemical Engineering or similar
- Knowledge in analytical methods and bioprocess technology of cell cultures
- Experience and skills in data analysis and statistical assessment of large data sets including strong background in mechanistic and hybrid modelling (Python, MATLAB®)
- Interest in working with complex cultivation set ups for next generation therapies combined with digitalization strategies
- Enthusiasm for transfer established methods of bioprocess characterization to the emerging field of Cell and Gene Therapy

- Affinity for the power of data science and digital twins to allow affordable drugs for the world
- Willingness to travel to project meetings and scientific conferences
- Excellent English language skills in scientific field
- Personal skills: You should be accustomed to networked and critical analytical thinking, scientifically interested and able to independently work in a team.