

Developing a smart bioprocessing platform for personalised autologous cell therapies

17th Annual Bioprocessing Summit

Patrick Statham

Boston | 21st August 2025

We are an independent innovation and technology organisation committed to the advancement of cell and gene therapies



Our vision

A thriving industry delivering life-changing advanced therapies to the world.



Our role

Create powerful collaborations which overcome the challenges to the advancement of the ATMP sector.



How we work

We are a team of experts covering all aspects of advanced therapies. Applying our own unique capabilities and assets, we collaborate with academia, industry and healthcare providers to develop new technology and innovation.

Personalised Solid Tumour T-cell Therapy Platform

- Autologous processes are **complex**, **batch-to-batch** differences = **variable** performance, prone to **failure** and difficult to **scale**
- Therapies **costly** to produce,
 - Tecelra and Amtagvi currently **FDA approved** for treatment of solid tumours (**\$500-730k** per treatment)

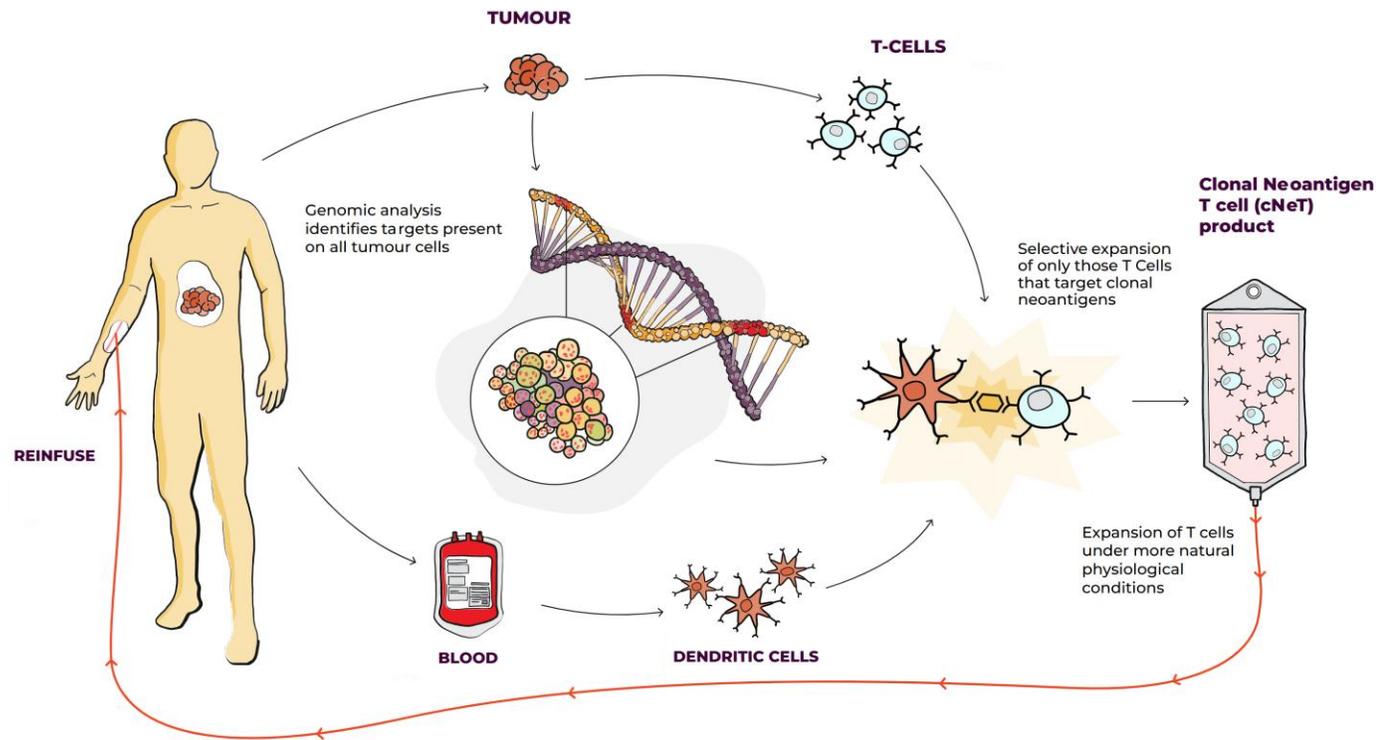


Figure 1: Exemplar adoptive TIL-therapy from Achilles Therapeutics PLC alongside the G-Rex100 system (Wilson-Wolf)

SMARTER Project

- 3-year **EU funded** consortium with three partners (UK/EU)
- **Aims:** To produce an **adaptive platform** which makes autologous cell therapy processes more **consistent** and **effective** by focussing on improved **efficiency, quality and scalability**

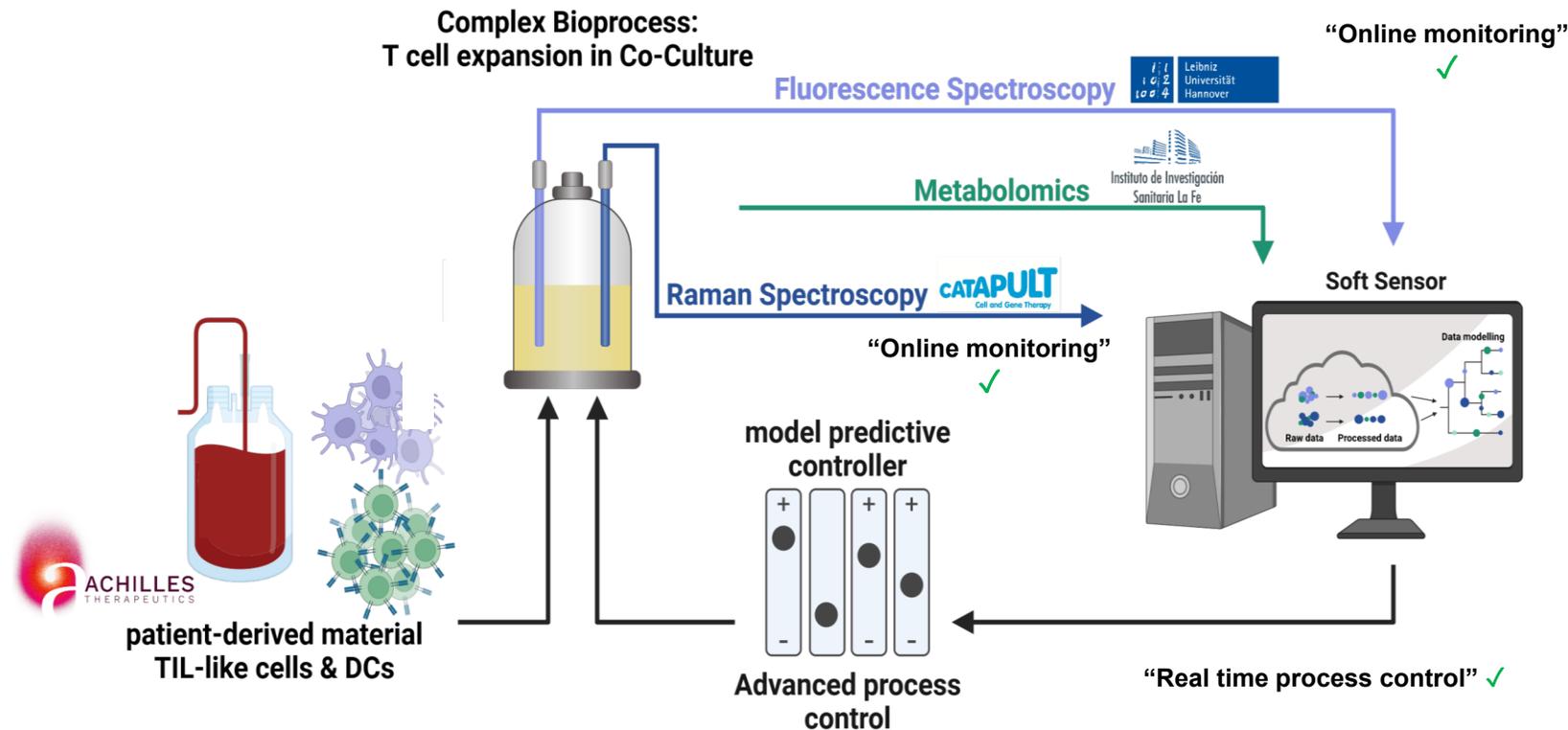
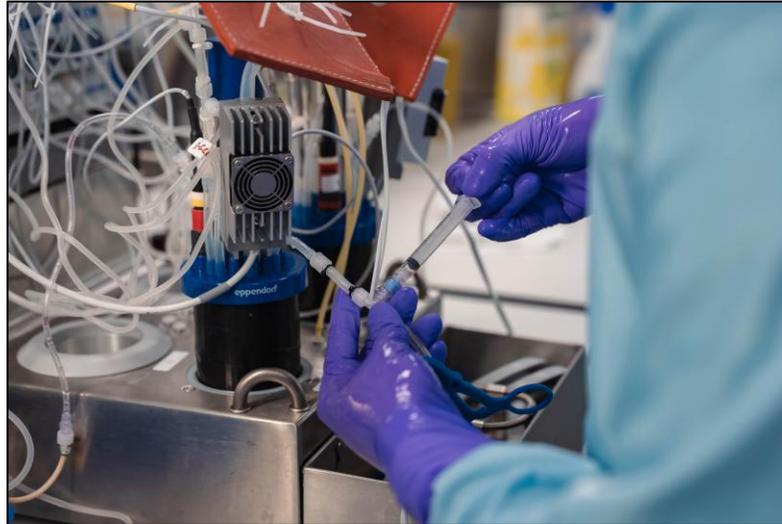


Figure 2: SMARTER consortium project structure

Why adapt from a static system to a dynamic process

Closed to operator intervention using **sterile** connections, and sterile sampling



Possible to **monitoring + control** process parameters (pH, O₂, agitation)

Modular device series facilitates ease of scale up/out

OPC-UA compatible, allowing real-time communication with digital systems



Compatible with CGTC/LUH **real-time PAT sensors**

Leverages **automation** to facilitate reduced manual labour and reduction in COGs

Objectives

Study 1: Adapt process to dynamic system

Study 2: Identify critical process parameters (CPPs) and novel biomarkers

Study 3: Explore design space to generate process understanding and robust chemometric and bioprocess models for use in process control

Study 4: Proof of concept process control

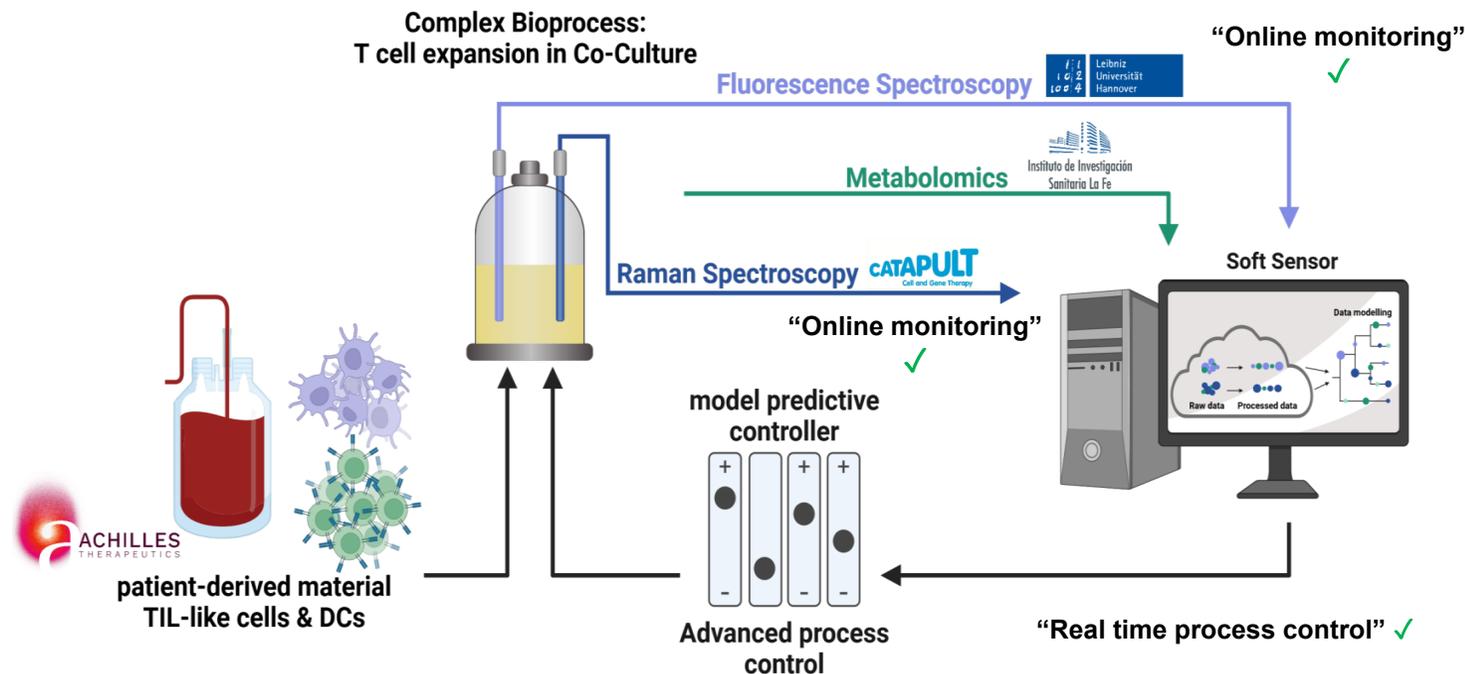
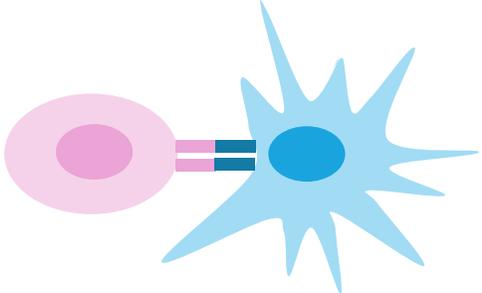
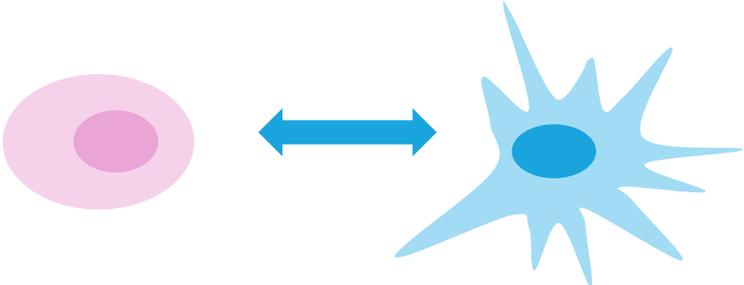


Figure 3: SMARTER consortium project structure

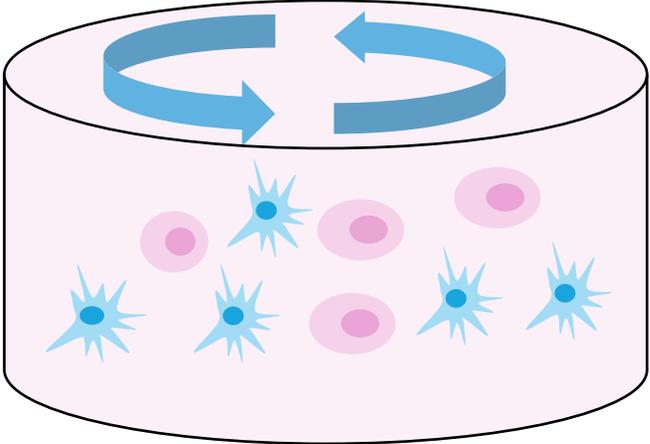
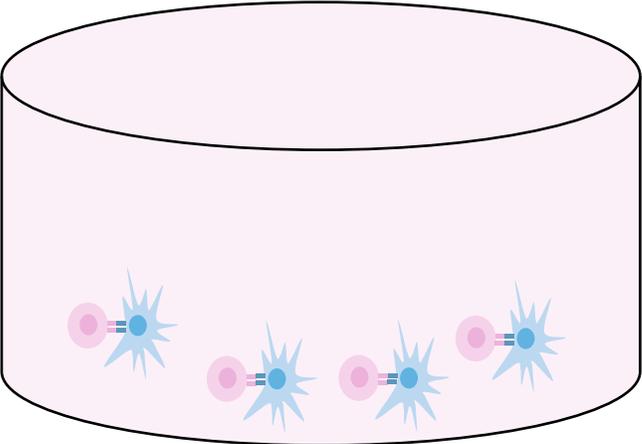
Study 1: Challenges transition from static to dynamic



Settling in static system promotes cells interaction



Agitating co-culture may inhibit interaction and induce cellular stress



Study 1: Static to dynamic adaptation

Investigating agitation regimes on T-cell process performance

Feeding Strategy

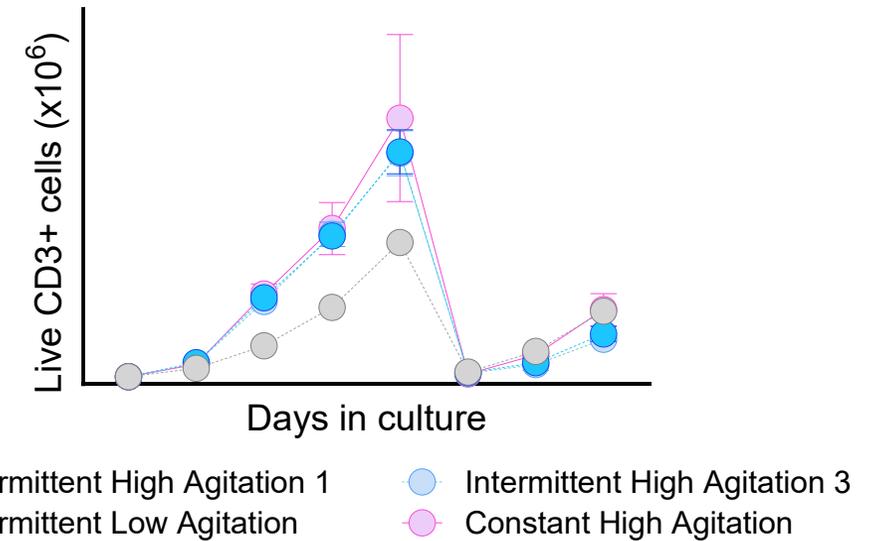
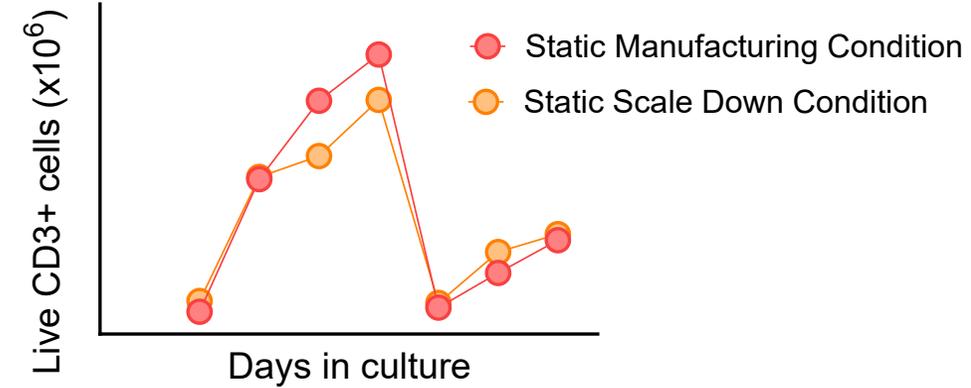
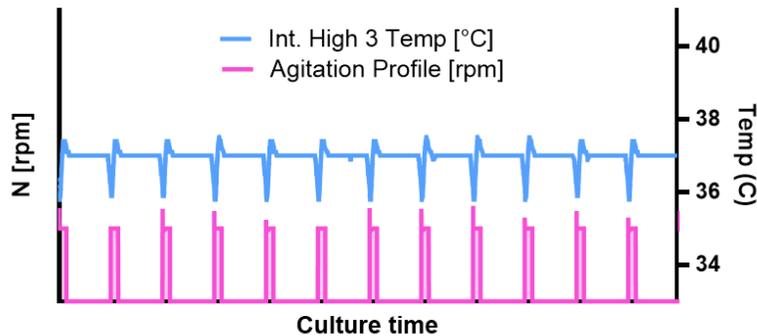
Media formulation and feeding strategy adapted to meet vessel volume constraints

Comparison of scaled process performed in sending party static bioreactor system

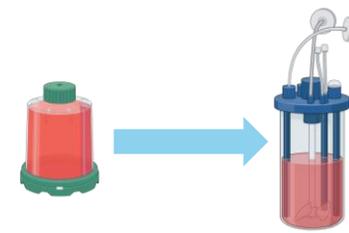
Bioreactor Setpoints

Intermittent and constant agitation profiles investigated at low and high RPMs to screen the impact on CQA's

DO (%), pH setpoint, gassing strategy all informed by prior CGTC know-how in immunotherapy bioprocessing

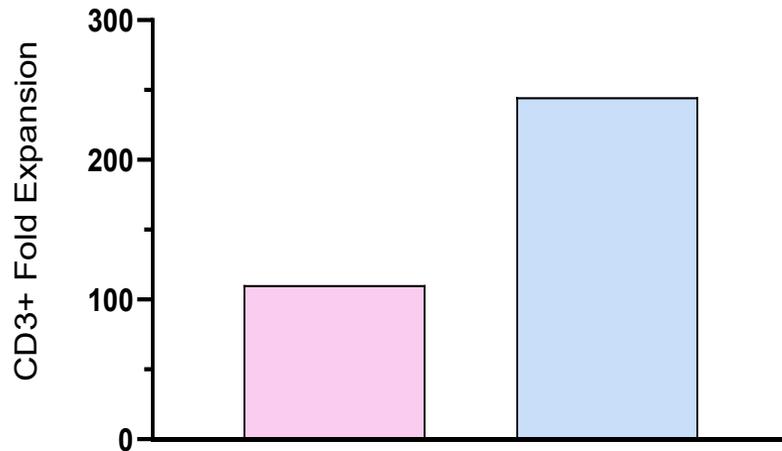


Study 1: Static to dynamic adaptation



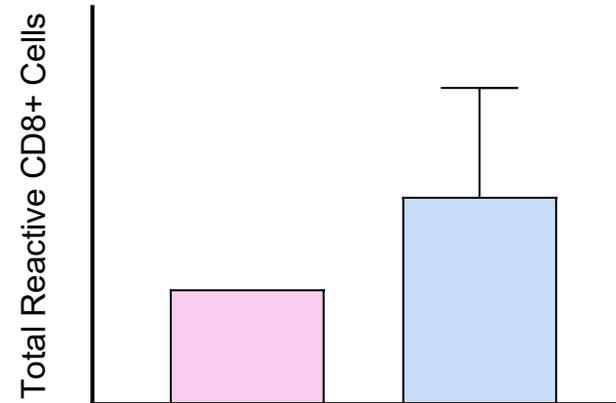
- CGTC known **critical process parameters** were adjusted to facilitate adaptation of the process into an **agitated suspension system**
- Initial dataset **challenged the prior-art** regarding co-culture for TIL antigen presentation
- Following initial adaptations, basic optimisations were made to improve the cell yields by **2.5x**, whilst maintaining critical **T-cell functionality and populations**

Improved Yields of CD3+



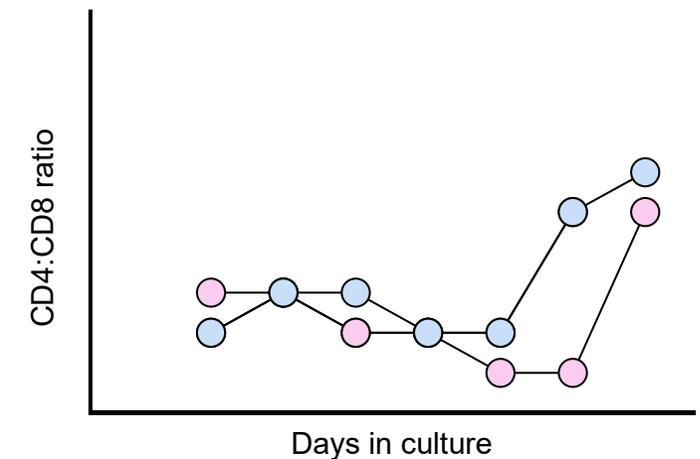
Collaborator Static Process
CGTC Dynamic Process

Maintenance of T-cell Reactivity to the antigen



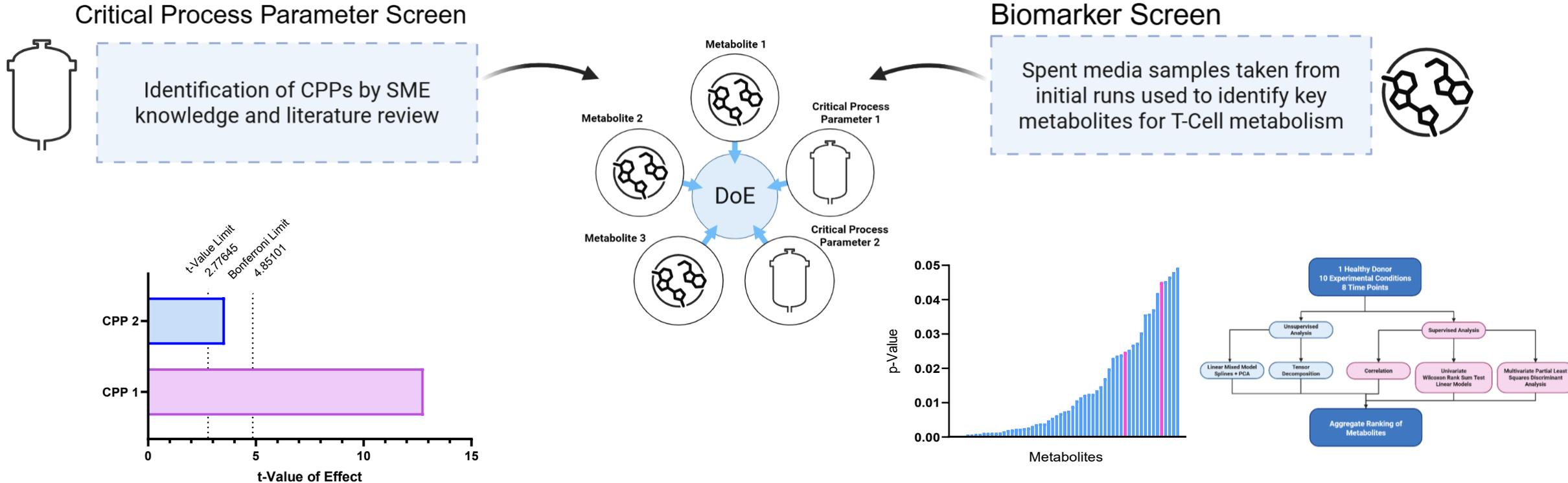
Collaborator Static Process
CGTC Dynamic Process

Comparable CD4:CD8 Ratio



Collaborator Static Process
CGTC Dynamic Process

Study 2: Critical Process Parameter Discovery



- 3 x 5 factor DoE runs performed
- Two CPPs with greatest influence over our process taken forward into 32 condition DoE

- Alongside Glucose, two other metabolites were identified:
 - Metabolite B: Involved in improved T-cell expansion
 - Metabolite C: Hypothesised to improve T-cell effector responses/reactivity

Study 3: Exploring the metabolic and dynamic parameter design space

- Metabolite and dynamic process parameters discovered in screening experiments taken forward into 32 vessel DoE, using a **central composite design** structure
 - Investigated **5-factors at 5-levels**
 - Performed over **4 x 8 vessel STR runs** at 0.3c scale
 - A **Raman Spectroscopy probe** was included for collection of spectra for chemometric modelling

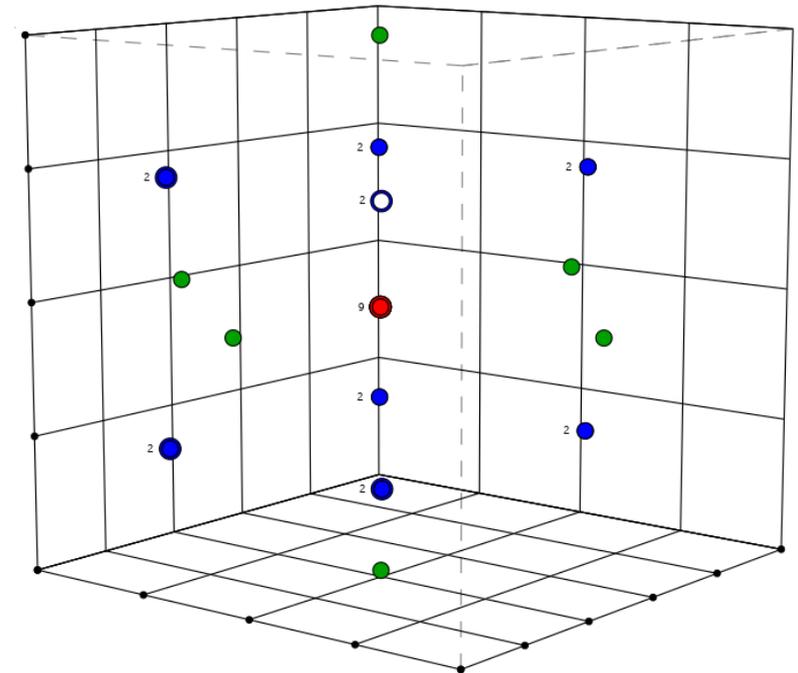
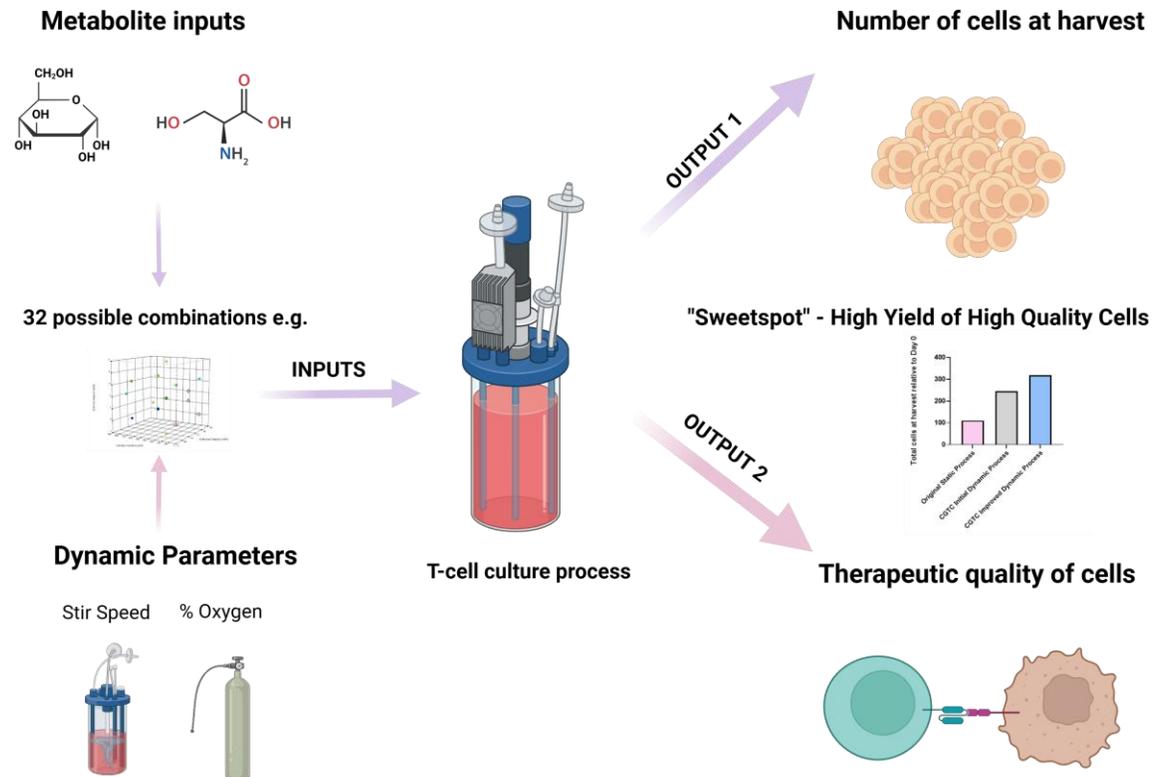
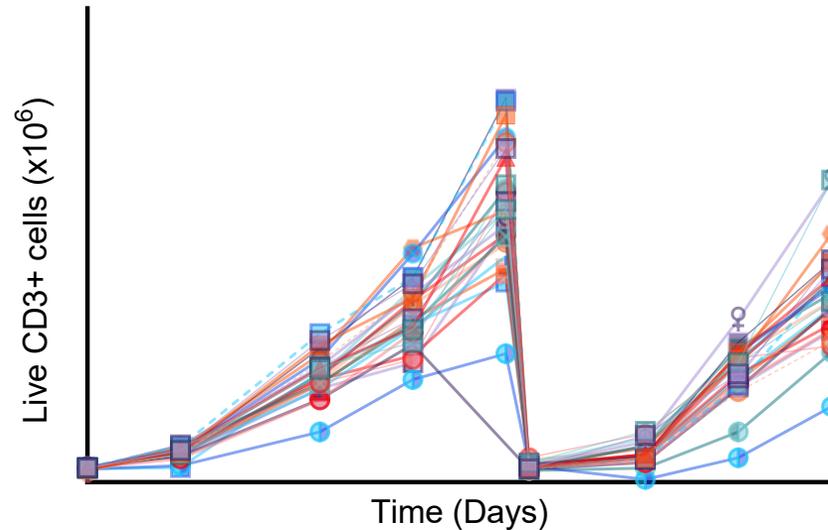


Figure 4: Study 3 Central composite design structure.

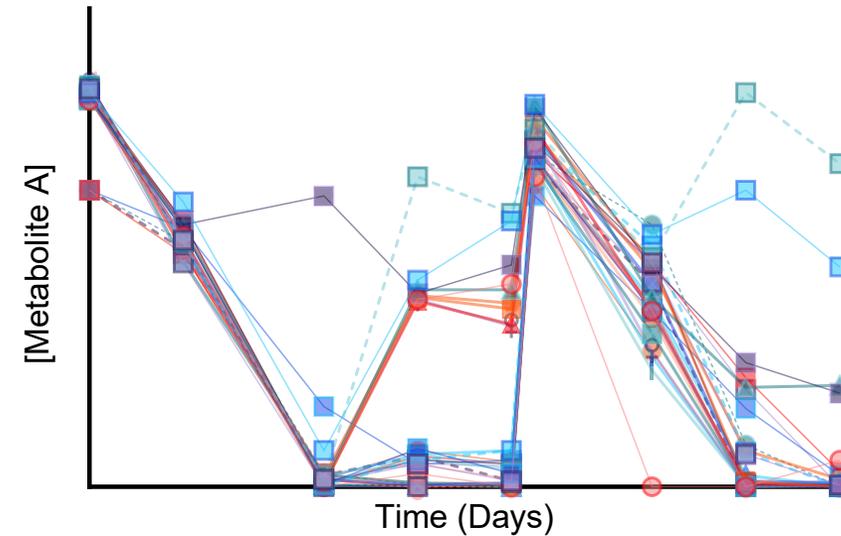
Study 3: Exploring the design space

Data collection

Cell expansion



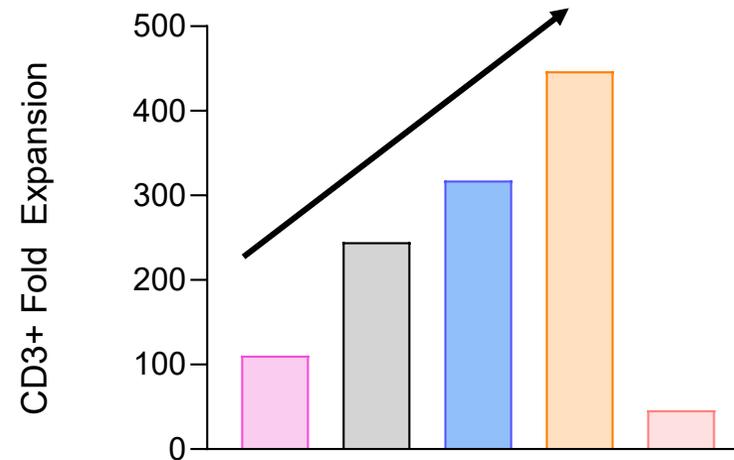
Metabolite profiles



- BD FACSLyric used to acquire [TBNK data](#) for cell [quantification](#) and phenotyping
- Offline [metabolite data](#) acquired at-line (BioFLEX2) and offline (LCMS)
- Spectral data was collected for use in [chemometric modelling](#)
- **4 key outputs set as response for DoE:**
 - CD3+ fold expansion
 - Reactive CD4+ fold expansion
 - Reactive CD8+ fold expansion
 - % Reactivity to the antigen

Study 3: Exploring the design space

Influence on T-cell process performance



- DoE model outputs showed **significant effect of chosen parameters** on the process
- Novel T-cell metabolic supplementation (**metabolite C**) demonstrated positive impact **on T-cell reactivity**
- DoE optimisation data will be utilised alongside **on-line PAT tools** to control at desired setpoints for **optimal process performance**

Study 3: Exploring the design space

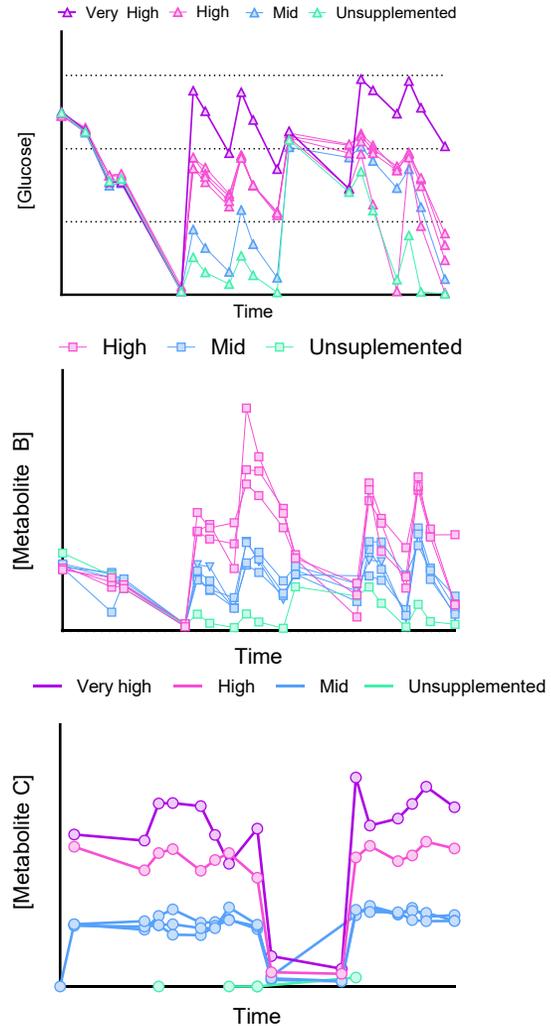
Optimisation of T-cell critical process parameters

Glucose setpoint	Metabolite B setpoint	Metabolite C setpoint	DO (%)	Agitation Speed (RPM)	Response
↑	↑	↓	↑	↓	CD3+ Fold Expansion
↓	↑	↓	↑	↑	Reactive CD4+ Fold Expansion
↓	↑	↓	↑	↑	Reactive CD8+ Fold Expansion
↓	↓	↑	↑	↑	% Reactivity

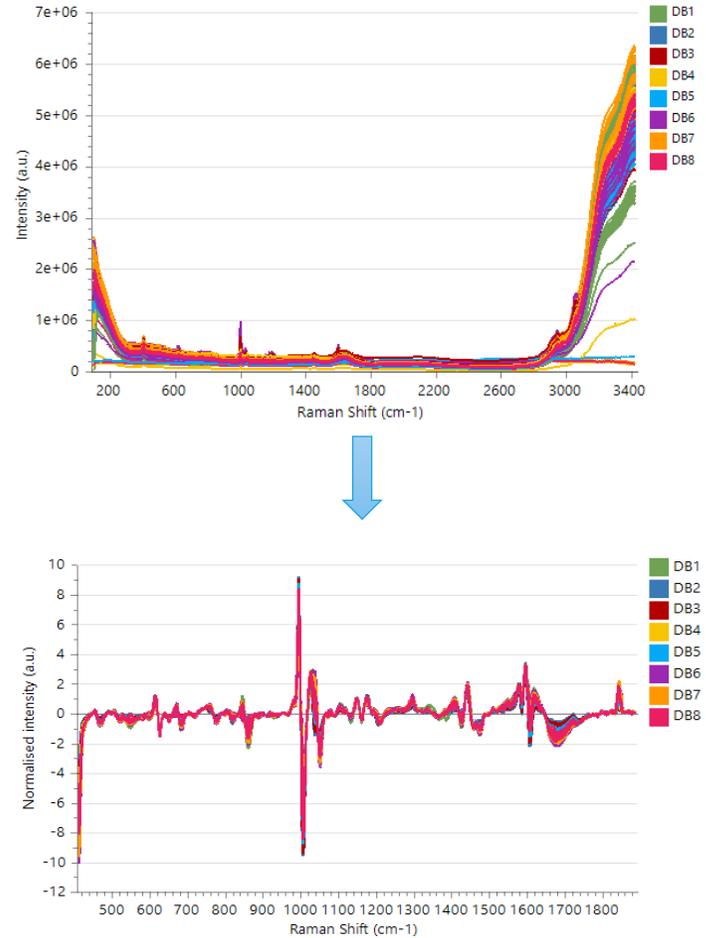
Study 3: Exploring the “design space”

Chemometric model generation process

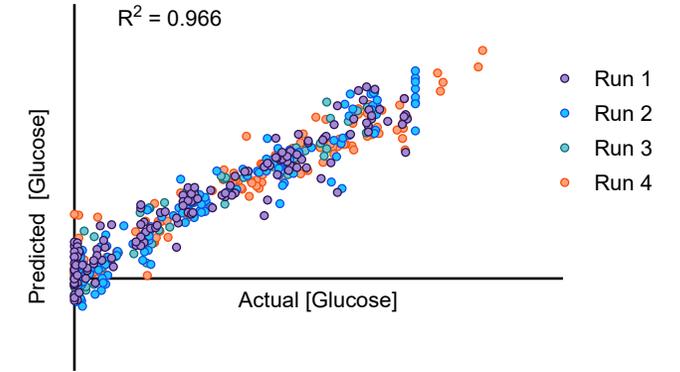
Metabolite perturbation and offline analysis



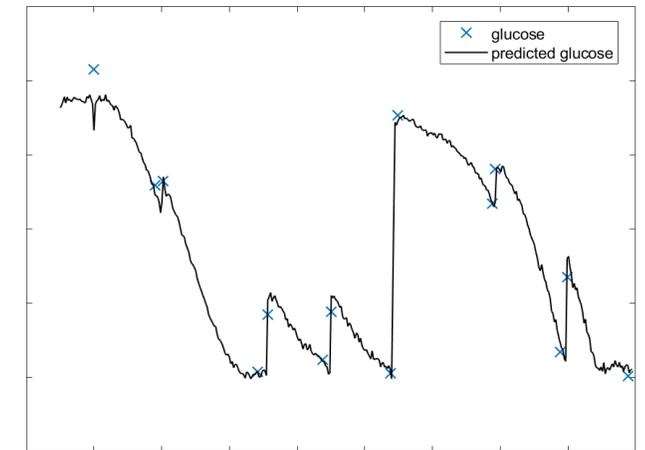
Spectra Collection and Processing



Glucose Model Generation and Testing



Real time Glucose monitoring



Study 4: Proof of concept process control

Chemometric based process control

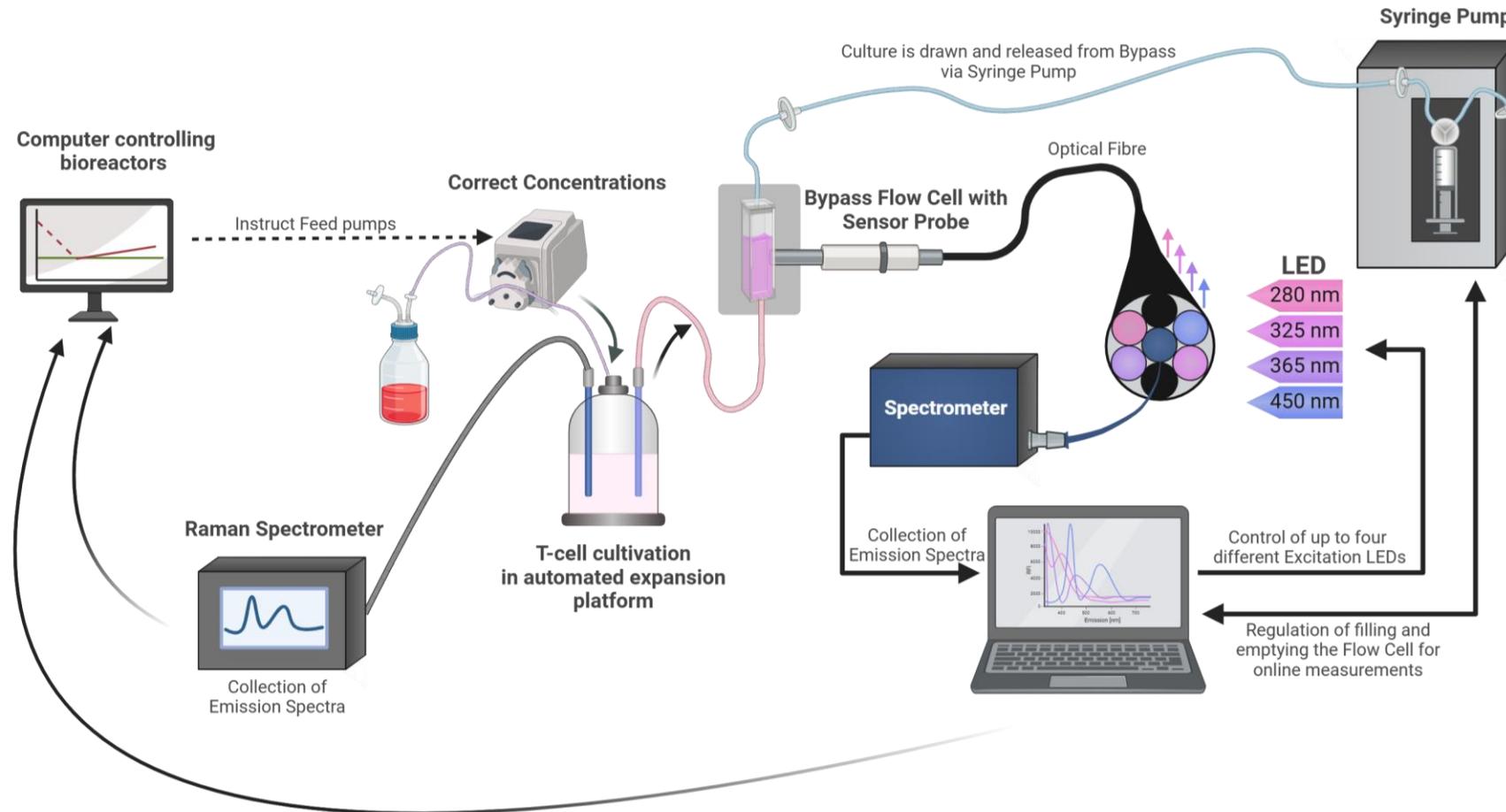
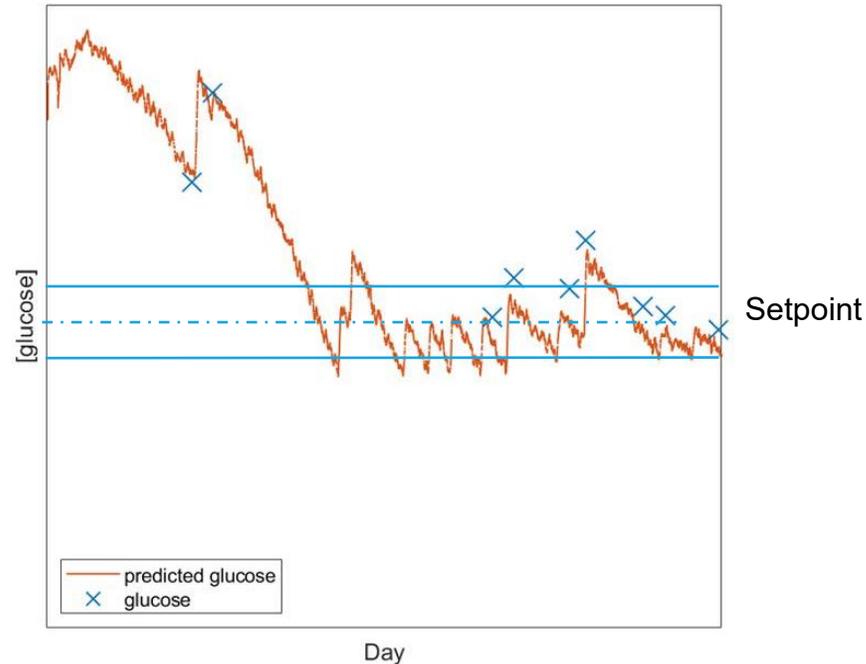


Figure 4: SMARTER project autologous proof of concept control architecture.

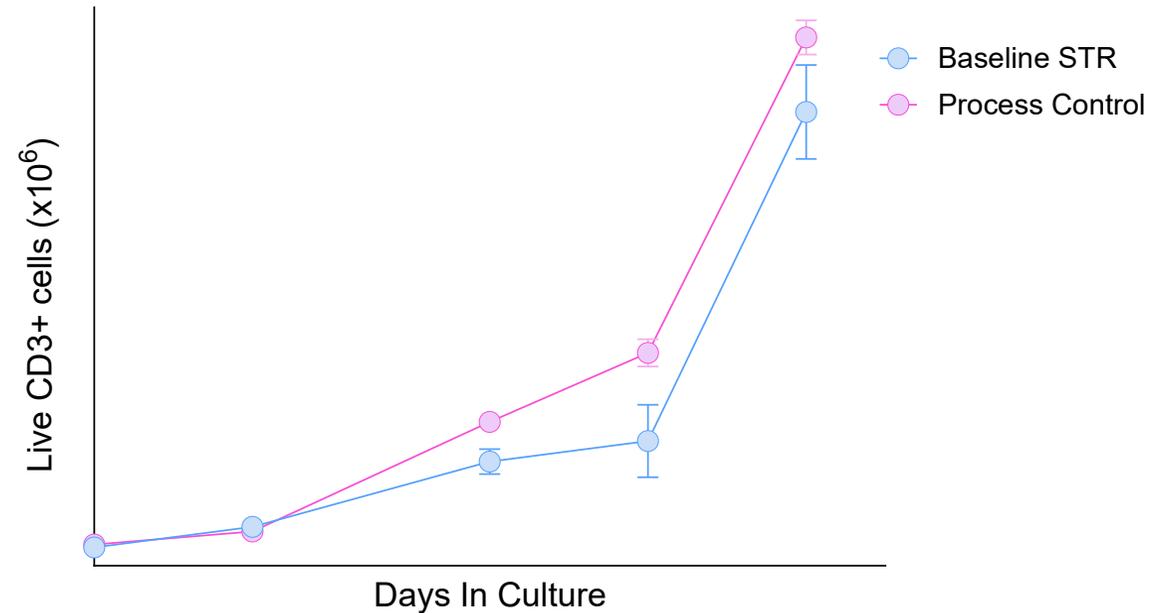
Study 4: Proof of concept process control

Chemometric based process control

Glucose Control



PoC Control Strategy Process Improvements



- PoC run used setpoints determined in DoE, alongside PID based control using PAT online data
- Run demonstrated trend towards improved performance based on control strategy

Conclusions and Future work

Perspectives for cell therapy manufacturing

Study Achievements

- Developed a roadmap for PAT informed advanced process control for autologous TIL process
- Enables increased consistency of manufacturing inherently variable cell therapy products
- Final WP to test patient material in system

Lessons

- Process analytical technologies (PAT) had limited sensitivity for some biomarkers identified in the screening exercise
- Approach limited to metabolites
- Exploration for next-generation screening approaches such as intensified DoE (iDOE) and hybrid modelling
- Improved cost-effectiveness in design space exploration activities and digital twin creation

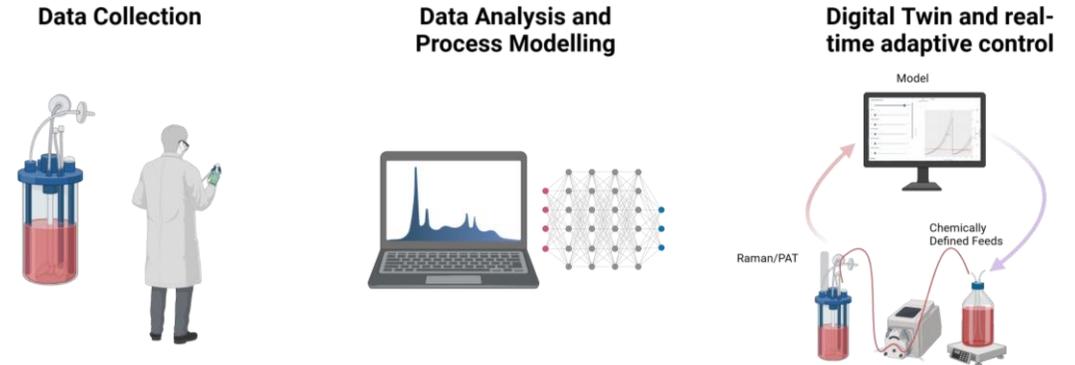


Figure 5: Roadmap of activities development of an adaptive control strategy

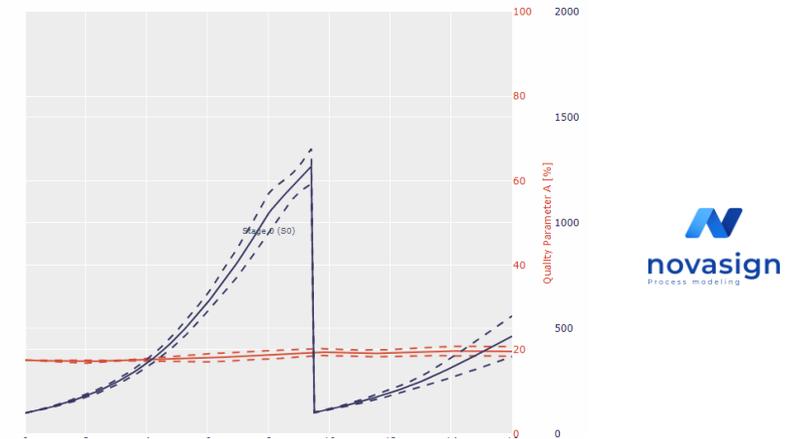


Figure 6: iDOE informed digital twin for autologous TIL process

Questions?

Acknowledgements:

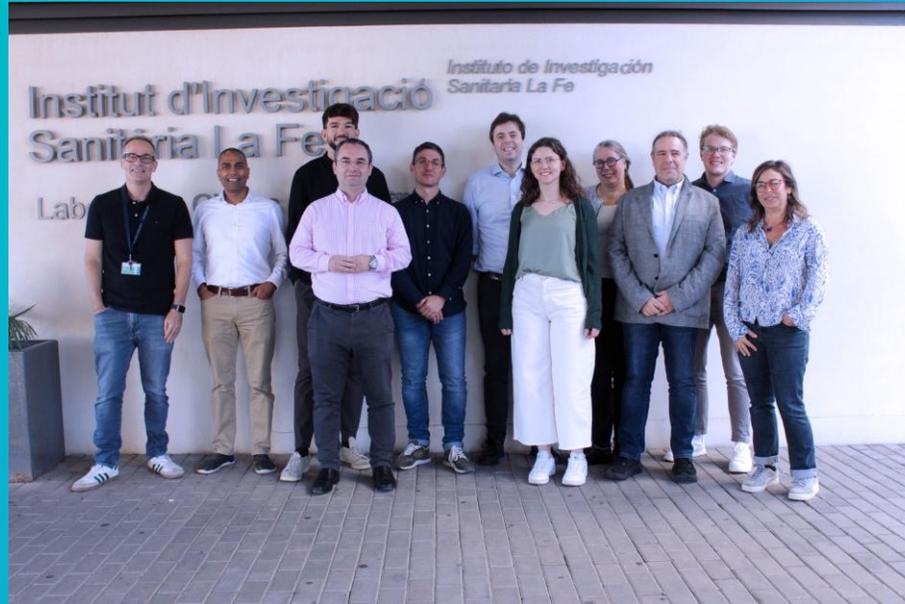
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Co-funded by
the European Union



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This work is supported by EU Horizon Europe Programme [grant number: 101071054] and Innovate UK [grant number: 10048117]"

18/02/2026