Developing a smart bioprocessing platform for personalised autologous cell therapies

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Patrick Statham

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Personalised Solid Tumour T-cell Therapy Platform

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

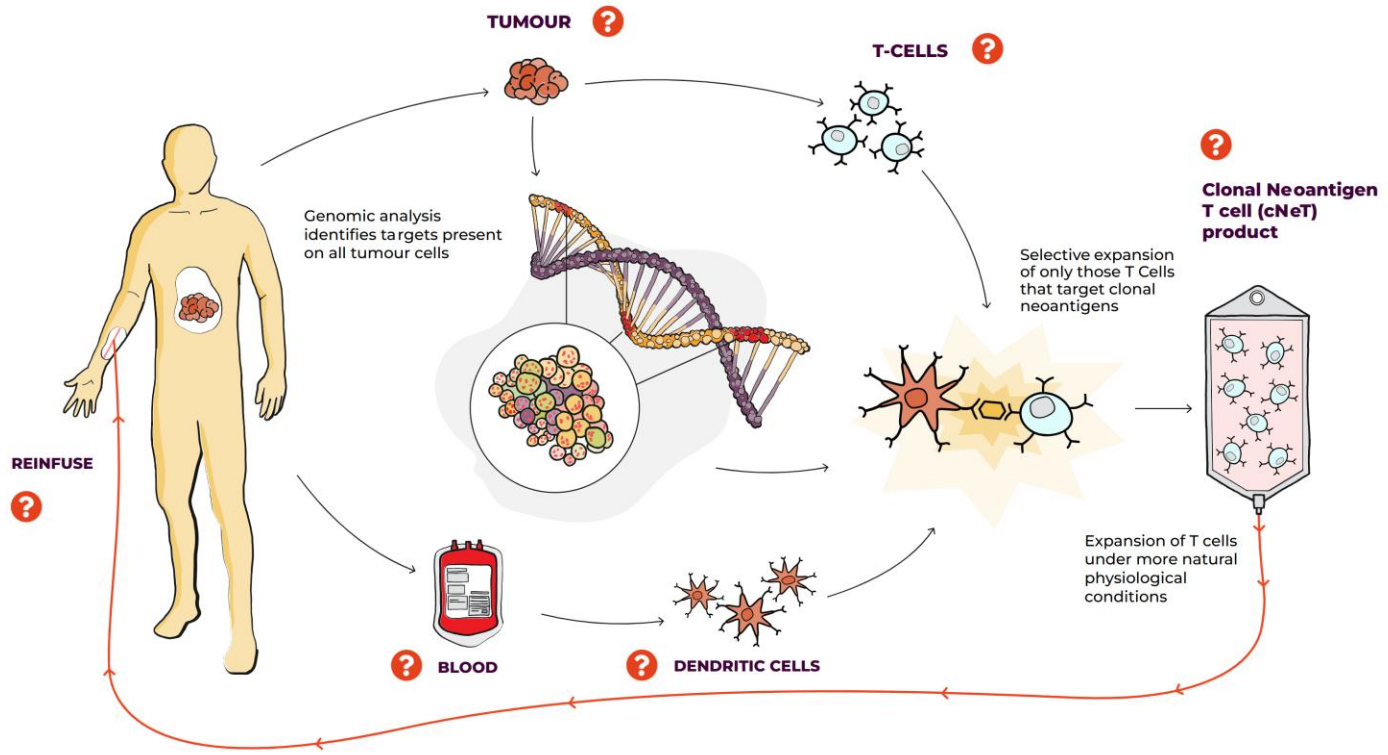
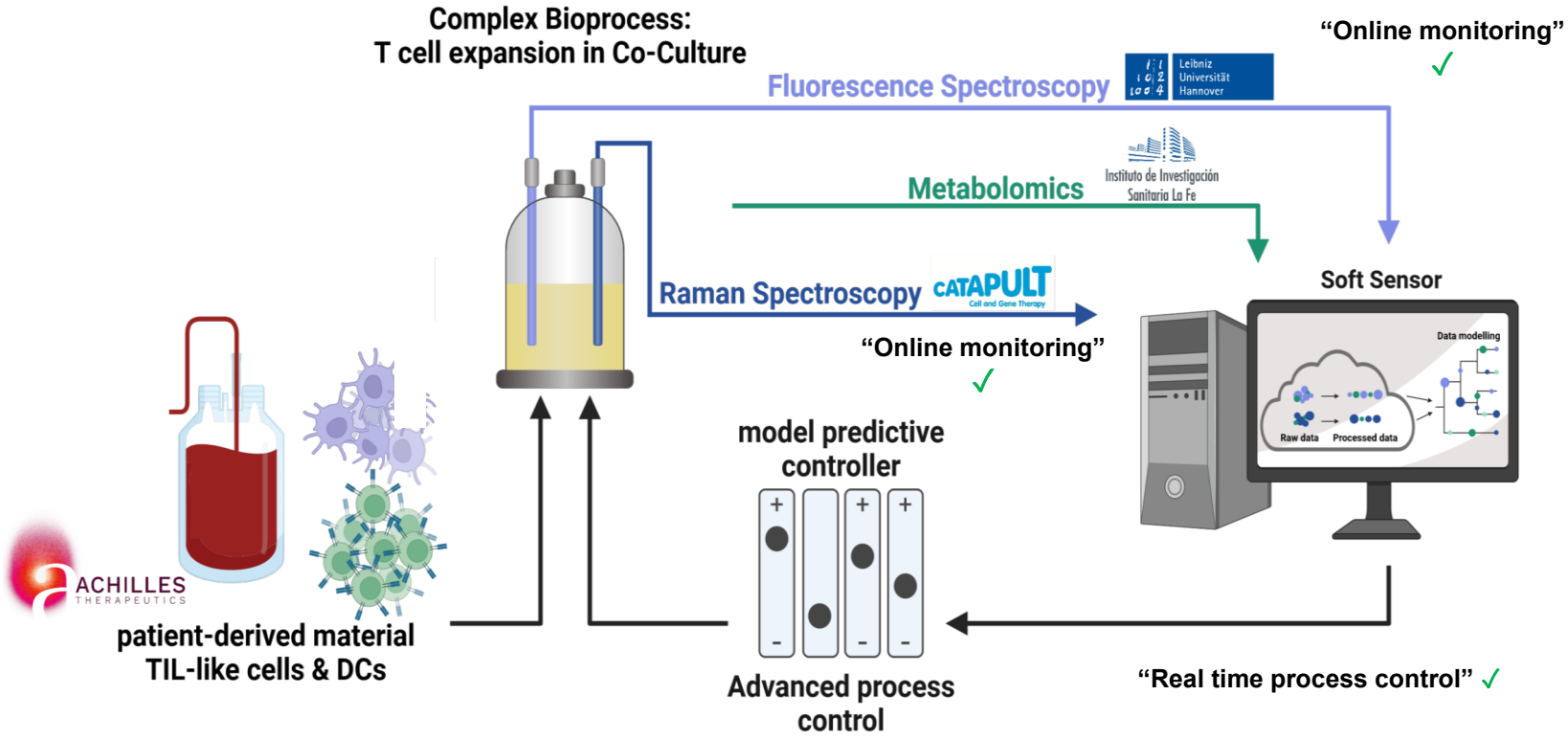


Figure 1: *Exemplar adoptive TIL-therapy from Achilles Therapeutics PLC alongside the G-Rex100 system (Wilson-Wolf)*

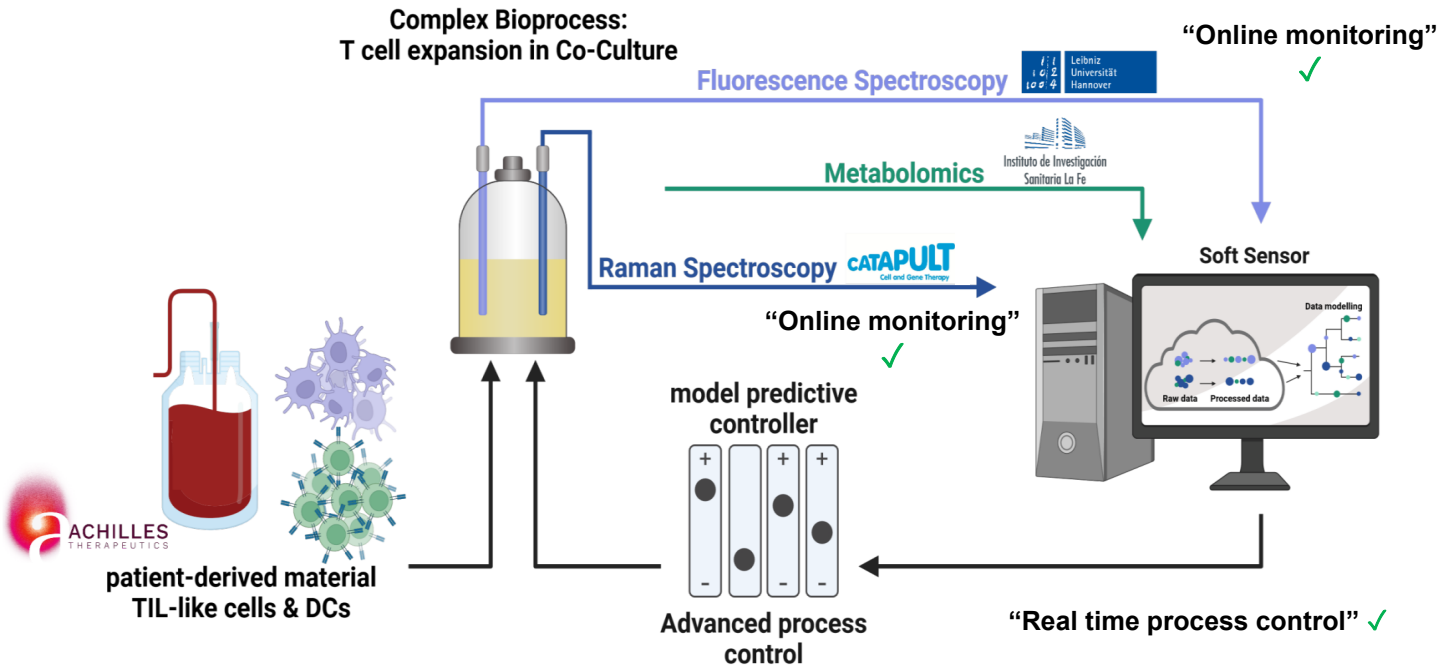
SMARTER Project

- **Aims:** To produce a platform which makes autologous cell therapies more **accessible** and **effective** by focussing on improved **efficiency, quality and scalability**

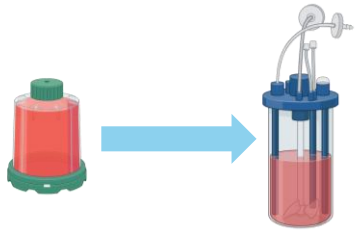


Objectives

1. Adapt process to dynamic system
2. Identify critical process parameters (CPPs) and novel biomarkers
3. Explore design space to generate process understanding and robust chemometric and bioprocess models for use in process control

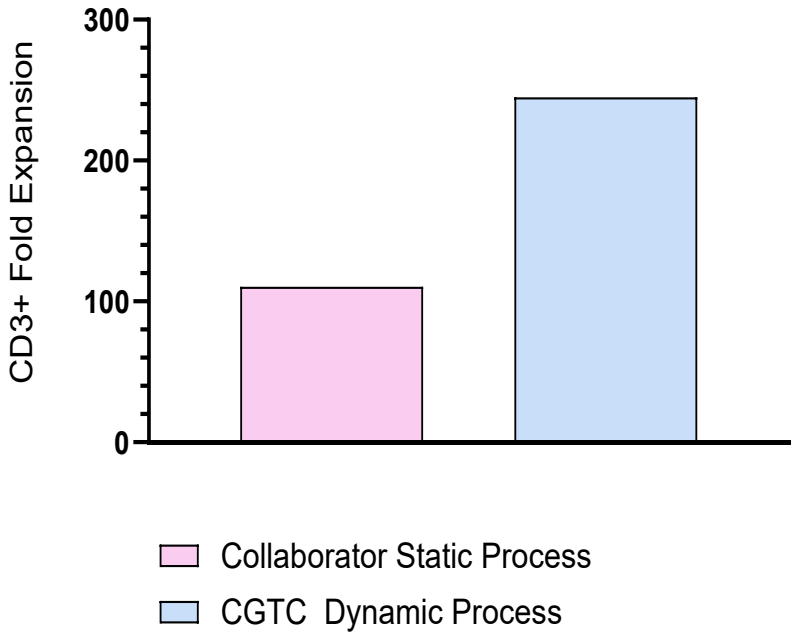


Study 1: Static to dynamic adaptation

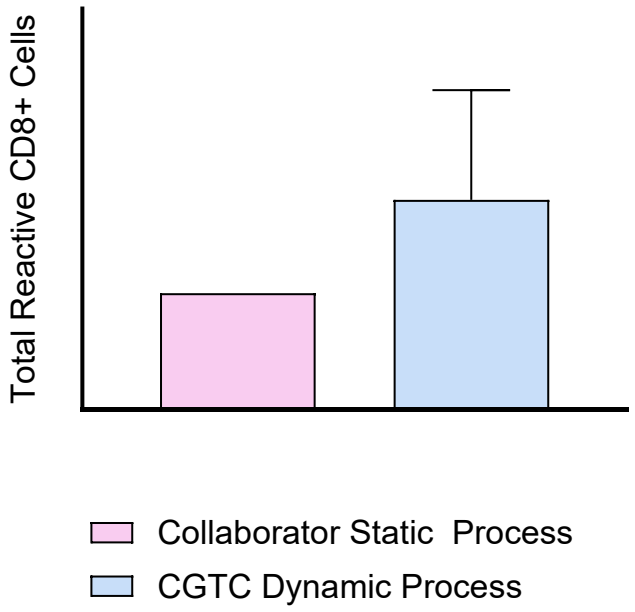


- CGTC known critical process parameters were adjusted to facilitate adaptation of the process into an agitated suspension system
- Initial dataset challenged the prior-art regarding co-culture for TIL antigen presentation
- Following initial adaptations, basic optimisations were made to improve the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

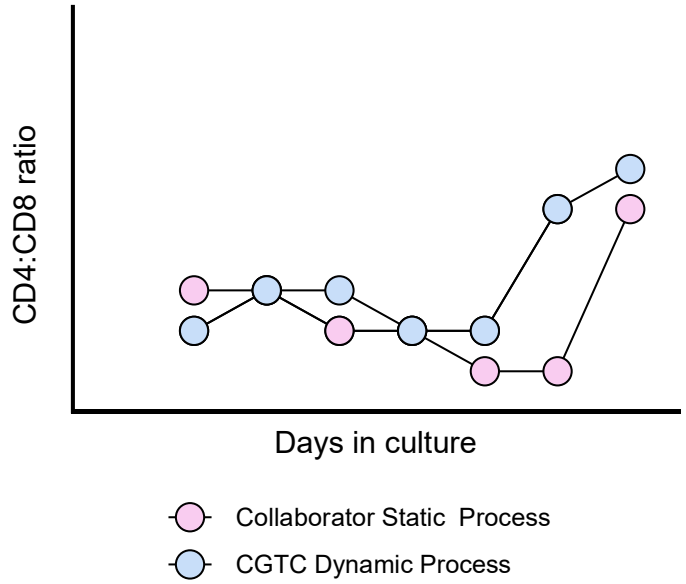
Improved Yields of CD3+



Maintenance of T-cell Reactivity to the antigen



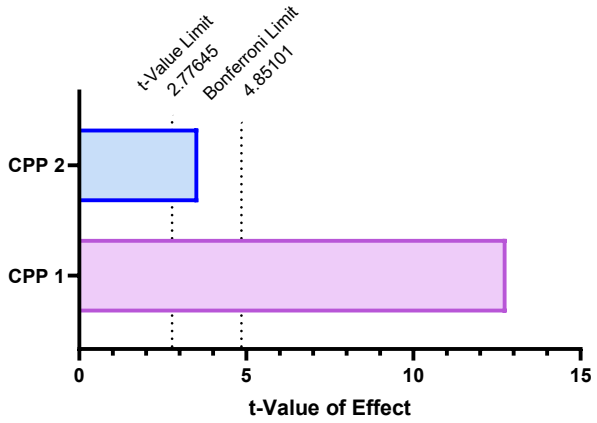
Comparable CD4:CD8 Ratio

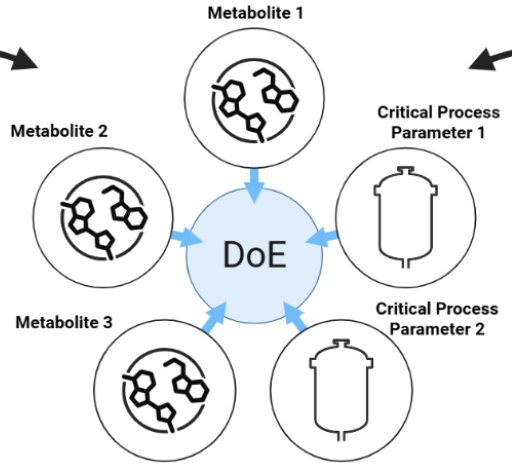


Study 2: Critical Process Parameter Discovery

Critical Process Parameter Screen

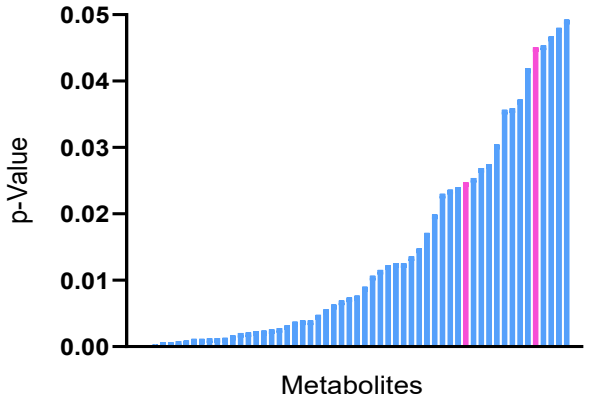
Identification of CPPs by SME knowledge and literature review





Biomarker Screen

Spent media samples taken from initial runs used to identify key metabolites for T-Cell metabolism

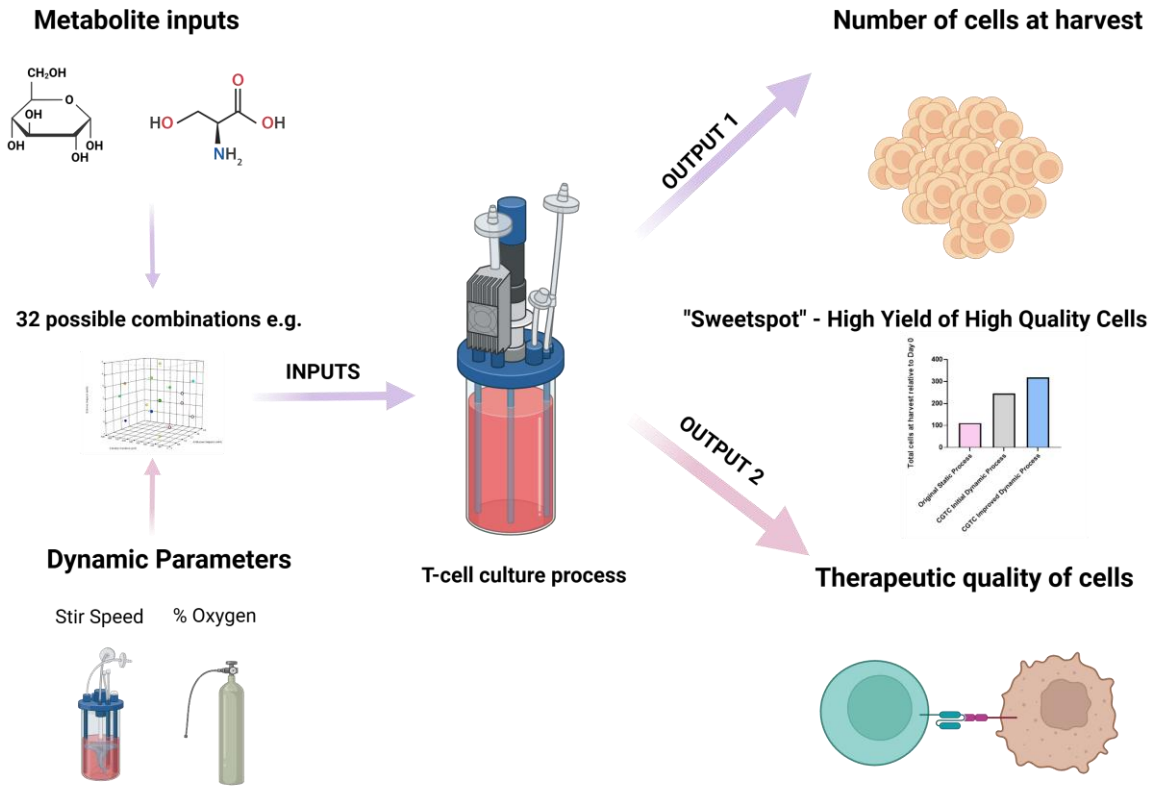


- 3 x 5 factor DoE runs performed
- Two CPPs with greatest influence over our process taken forward into 32 condition DoE

- 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 “design space”

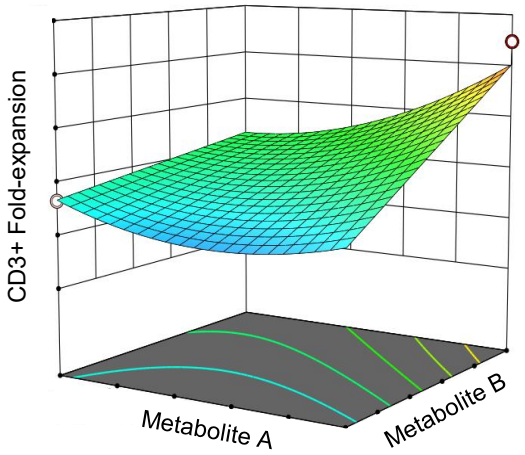
- Metabolite and dynamic process parameters discovered in screening experiments taken forward into 32 vessel DoE, using a central composite design structure
  - Investigated 5-factors at 5-levels
  - Performed over 4 x 8 vessel STR runs at 0.3c scale
  - A Raman Spectroscopy probe was included for collection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



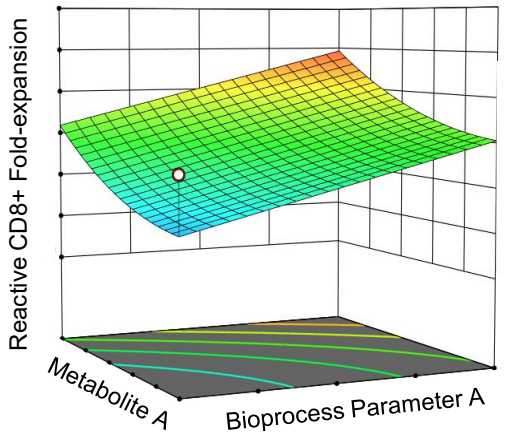
Study 3: Exploring the “design space”

Influence on T-cell process performance

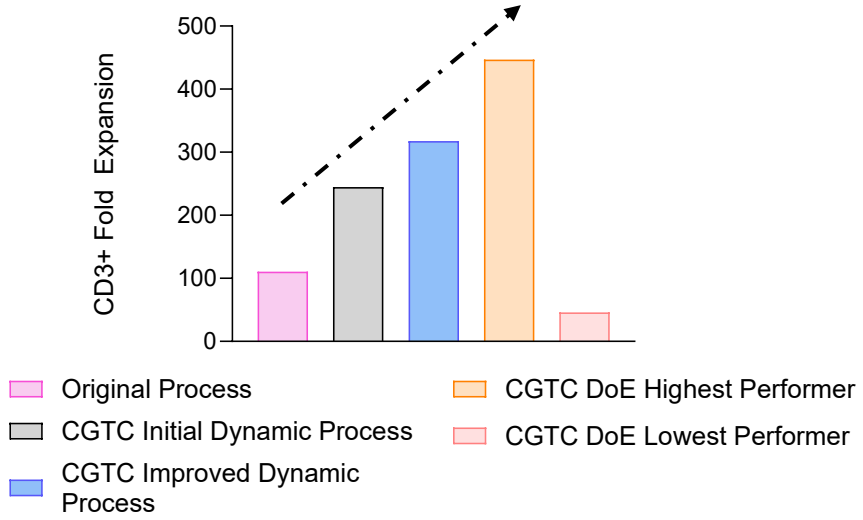
Metabolite A & B improve CD3+ expansion



Bioprocess parameter impact on Reactive CD8+ Fold-expansion



Further Process Optimisation

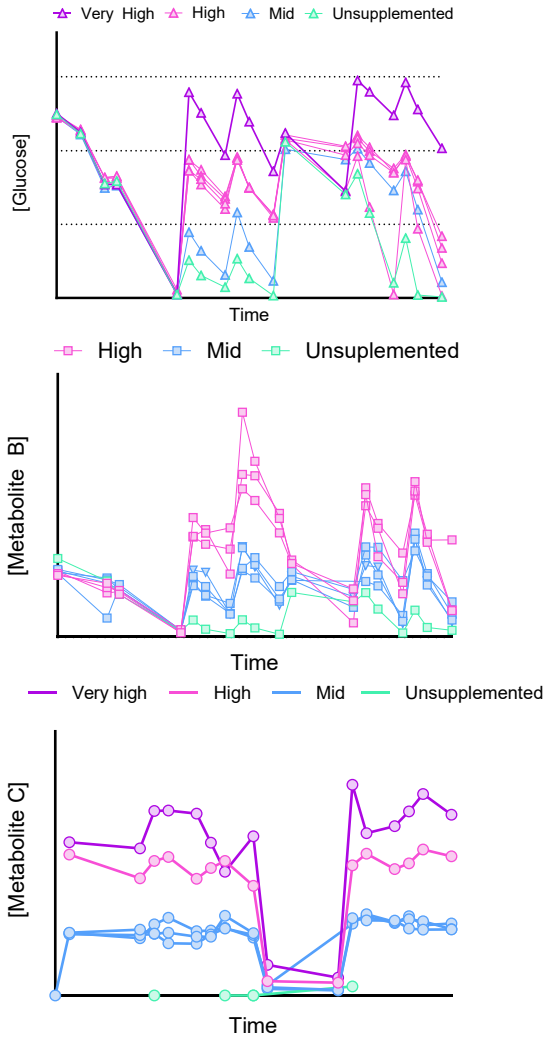


- DoE model outputs showed significant effect of chosen parameters on the process
- Novel T-cell metabolic supplementation (metabolite C) demonstrated positive impact on T-cell reactivity
- DoE optimisation will be utilised alongside on-line PAT tools to control at desired setpoints for optimal process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

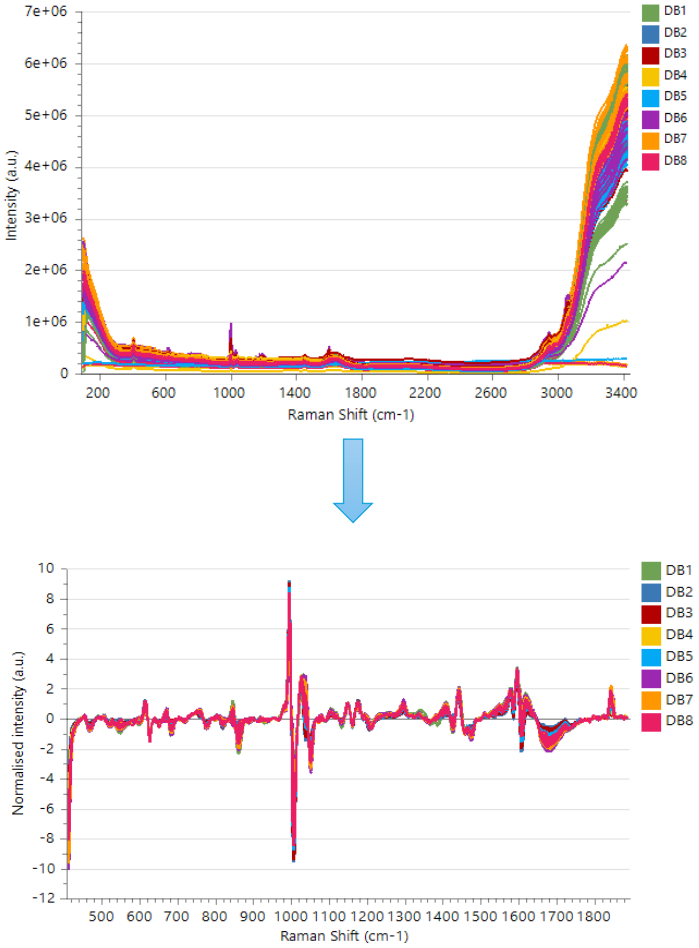
Study 3: Exploring the “design space”

Chemometric model generation process

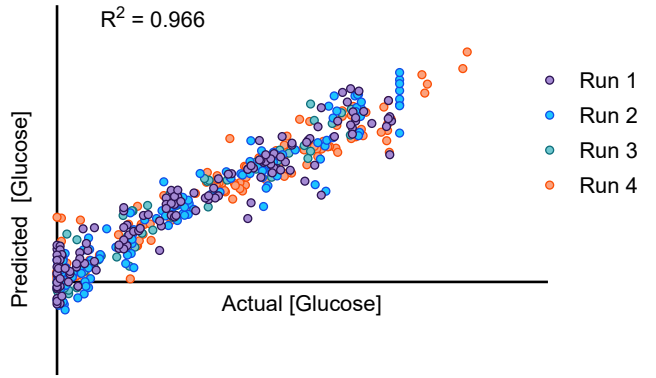
Metabolite perturbation and offline analysis



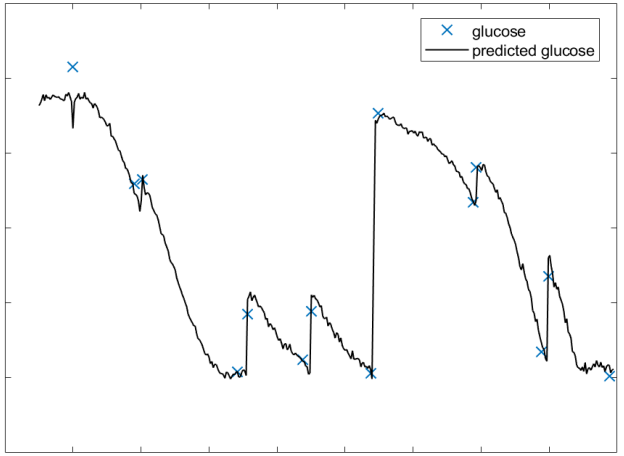
Spectra Collection and Processing



Glucose Model Generation and Testing

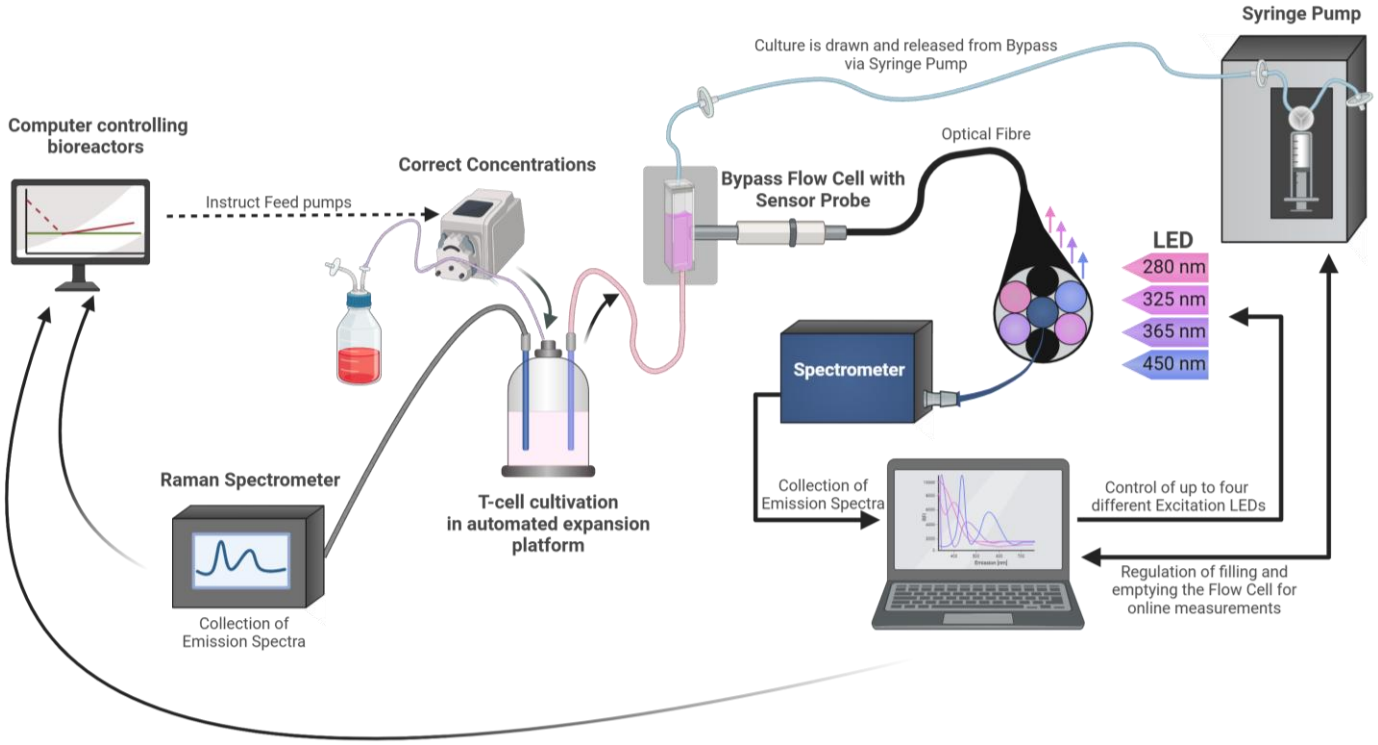


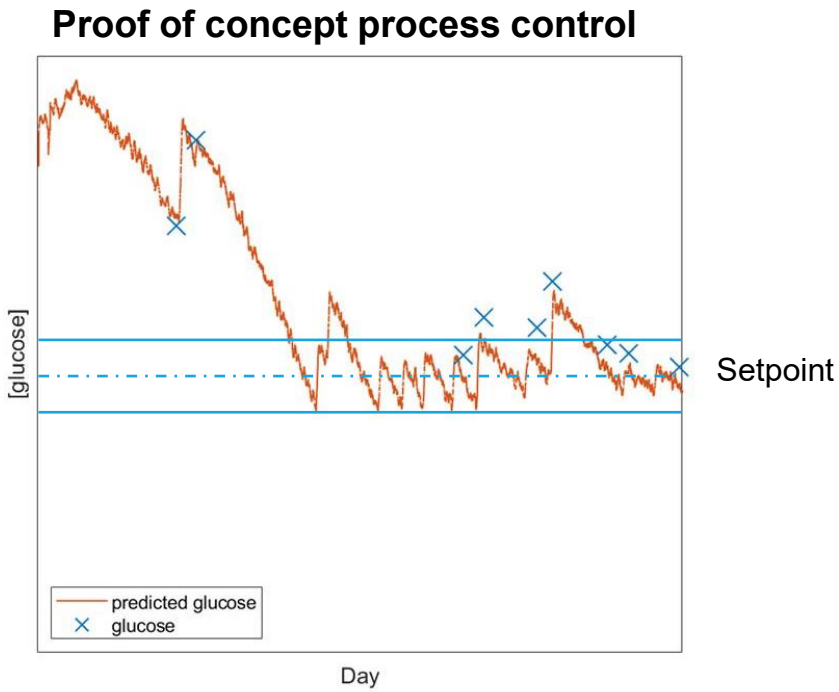
Real time Glucose monitoring



Conclusions and next steps

- Successfully adapted a static autologous process into an agitated system capable of real time monitoring and control
- Evidence for novel metabolite and bioprocessing approaches to producing high yields of T-cells with therapeutic potential
- Next steps to develop a control model and integrated this into a proof of concept run with patient material





Developed a roadmap from static systems to proof of concept automated and digitalised processes

Questions?

Acknowledgements:

CGTC Team

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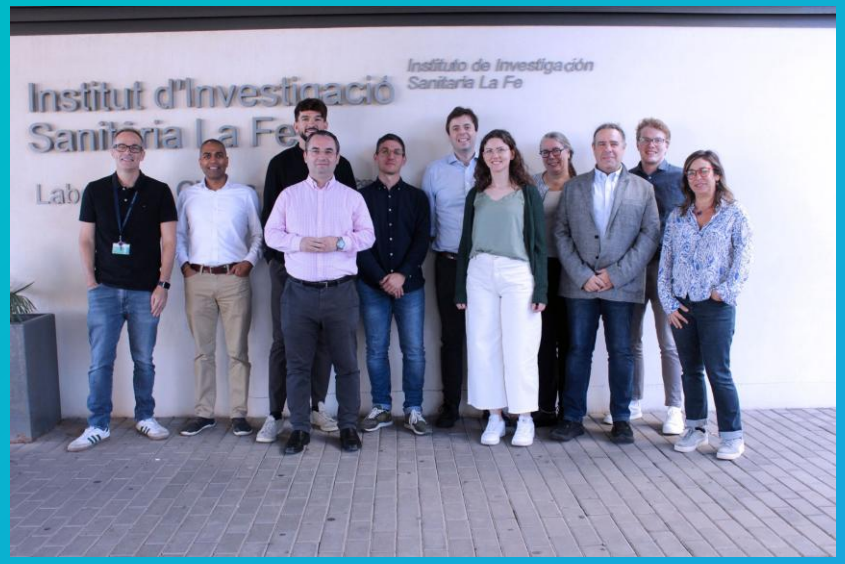

Catapult Team

12th Floor Tower Wing
Guy's Hospital
Great Maze Pond
London SE1 9RT

info@ct.catapult.org.uk
ct.catapult.org.uk
LinkedIn: cgt-catapult

https://smarter-project.eu/

Email: patrick.statham@ct.catapult.org.uk