

WP-leader

Pontus Blomberg, Karolinska University Hospital

Partners

Karolinska Institutet, KTH, RISE, Region Uppsala, Pfizer, Cytiva, Xintela, Boobicell, Cell Seed, TATAA Biocenter, Region Stockholm, Region Skåne, Region Västerbotten, Region Östergötland and Region Örebro län.

WP2 Projects

2-1 Developing a Pre-GMP facility for vectors and genetically modified cells

Karolinska Institutet (PL-Sällberg), Karolinska Universitetssjukhuset, Cytiva, RISE.

2-2 Vecura - An Infrastructure for Development and Manufacturing of ATMPs

Karolinska (PL-Blomberg), KI, Uppsala university, RISE, GEHC, CellSeed AB.

2-3 Expansion of GMP Compliant Tumor Infiltrating Lymphocytes (TILs) in Xuri bioreactor

Karolinska (PL-Blomberg), KI, Cytiva.

2-4 Harmonizing HQ plasmid production between pre-GMP and GMP sites,

Karolinska Institutet (PL-Sällberg), Karolinska Universitetssjukhuset, Cobra Biologics, Svenska vaccinfabriken AB.

2.1 - Developing a Pre-GMP facility for vectors and genetically modified cells



Partners:  **cytiva**



 **KAROLINSKA**
UNIVERSITETSSJUKHUSET

RI
SE

Q3 2018 – Q2 2021

Aim:

- Set up and equip the Pre-GMP facility for the development of SOPs for production of gene modified T cells

Methods/technologies:

- Plasmid production using disposable tanks
- DNA and RNA transfection of human PBMC
- Lentiviral production and transduction of human PBMC with T cell receptor genes targeting hepatitis C

2.1 - Developing a Pre-GMP facility for vectors and genetically modified cells

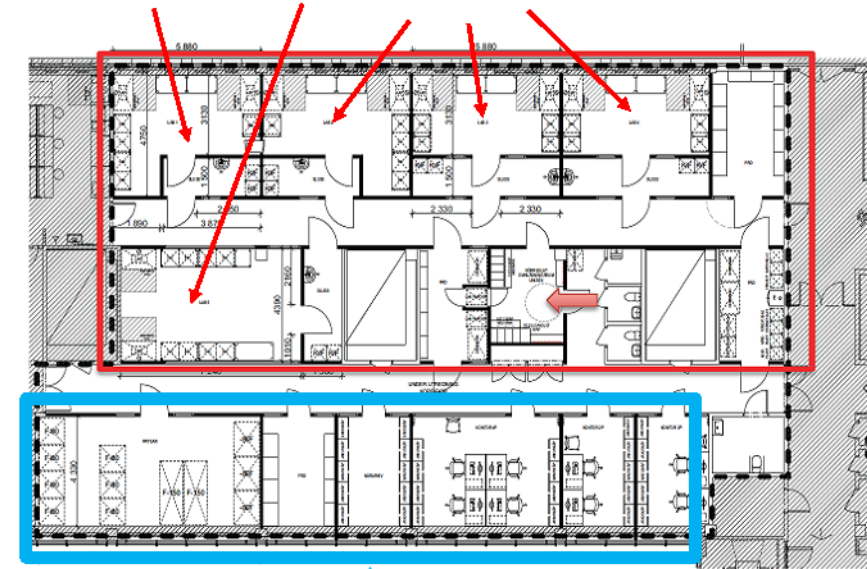
Results/Achievements:

- Eppendorf fermentor purchased and installed
- Milteny Prodigy with electroporator (first in the EU) in use
- First generation of TCR-T cells have been produced
- 4/5 clean rooms are currently occupied

Presentation and publications:

- Anna Pasetto (Facility Director) presented the facility at the CAR-TCR Summit meeting in London Feb 24-26, 2020
- Five publications

5 fully equipped clean rooms for: cell expansion, vector and plasmid production and purification, multiple projects



Office and archive space

2.2 - Vecura - An Infrastructure for Development and Manufacturing of ATMPs



Partners:



Q1 2018 – Q4 2020

Aims:

- Set up manufacturing processes compliant with EU-regulations
- Manufacture GMP-products
- Completed clinical trials using Vecura-site products

Methods/technologies:

- GMP-manufacturing (*Clean rooms, GMP-adaptation of manufacturing processes, Establishment of batch records, Regulatory support*)



Results/Achievements:

Manufacturing of CAR T Cells for B-cell malignancies (ongoing programme, >30 patients treated)

PIs: Gunilla Enblad and Magnus Essand, Uppsala

Manufacturing of TILs in bioreactors (Xuri)

PI: Rolf Kiessling, Karolinska Institutet

Established GMP protocol for manufacturing of IPS-cells

PI: Anna Falk, Karolinska Institutet

Established GMP compliant hESC bank

PI: Fredrik Lanner, Karolinska Institutet

Manufactured Mesenchymal Stroma Cells for ARDS/Covid-19

PI: Oscar Simonson, Akademiska Sjukhuset, Uppsala

Establishment of GMP manufacturing of keratinocytes for treatment of burn injuries (ongoing, tech transfer phase)

PI: Folke Sjöberg, Linköping

4 publications and 2 manuscripts

2.3 - Expansion of GMP Compliant Tumor Infiltrating Lymphocytes (TILs) in Xuri bioreactor



Partners:



Q1 2018 – Q4 2019

Aims:

- MAT 02 Clinical Trial – Melanoma
 - PI: Rolf Kiessling and Maria Wolodarski (Karolinska and KI)
- GMP Manufacturing: CCK and Vecura

Methods/technologies:

Design of trial

- Cohort, A, receives only the TILs
- Cohort, B, receives TILs and also dendritic cell (DC) vaccine at three occasions

GMP manufacturing

- Cell expansion of TILs in a closed culture system; the Xuri Bioreactor provided by Cytiva



Pis: Rolf Kiessling and Maria Wolodarski

2.3 - Expansion of GMP Compliant Tumor Infiltrating Lymphocytes (TILs) in Xuri bioreactor



Results/Achievements:

- Slow inclusion due to efficient check point inhibitors
- Efficient response in in the TILs + DC vaccine group (cohort B).
 - Four responders
 - Two are now free of tumors
 - One has only a very small lesion left
- Optimization of the protocol have resulted in that the latest patients all have been infused with approximately 30 billion TIL cells.



2.4 – Harmonizing HQ plasmid production between pre-GMP and GMP sites



Partners:



Q3 2019 – Q2 2021

Aim:

- Harmonize HQ plasmid production between pre-GMP at KI and Cobra Biologics

Methods/technologies:

- Fermentor based production and downstream processing



Results/Achievements:

- Eppendorf fermentor purchased and installed
- Upstream protocol and instrumentation in place

Patent:

- New GTMP patent filed (SVF)

Future plans:

- Fermentation run planned for December 2020
- Establish protocol for downstream process