Personalised tumour trained lymphocytes derived from regional lymph nodes for treatment of colorectal cancer

Anne-Laure Joly, Erwan Le Maître, Ana Lukic, Sofia Berglund, Luigi Notari, Ola Nilsson, Guro Gafvelin and Hans Grönlund.

Highlights

We present a novel personalised tumour trained lymphocytes (pTTL) therapy.

- pTTLs can be applied in **any cancer** expressing targetable neoantigens by the use of PIOR Manufacturing®.

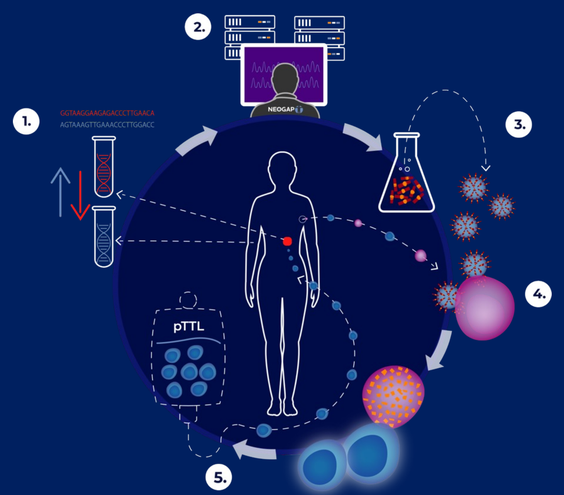
- Personalised therapy takes advantage of the **patient's own immune system**.

- The EpiTCer® technology offers a **novel** approach for **efficient antigen delivery** and specific T cell activation. Also applicable to the use of alternative starting materials.

- Despite individuals singularities, pTTLs are produced in a **reproducible** manufacturing process.

- pTTL are part of a **virtuous cycle**: every production linked to patient's tumour characteristics provides information to develop both process and product further.

pTTL production process overview



1. collection of tumour material and peripheral blood samples for next generation sequencing.
2. analysis of NGS data by in house software system PIOR Manufacturing® for neoantigen identification, selection and ranking.
3. production of EpiTCer® beads, including coupling of neoantigens to super-paramagnetic beads.
4. surgical collection of RLNs (starting material) and *in vitro* stimulation with EpiTCer® beads for pTTL expansion.
5. harvest and formulation. pTTL product is infused to the patient.

Background

We aim to develop a novel adoptive T cell therapy. pTTL therapy intends **to re-educate immune cells** to **eradicate tumour cells regardless of cancer type.**

pTTLs consist of regional lymph node (RLN) **tumour-antigen selected expanded T cells**.

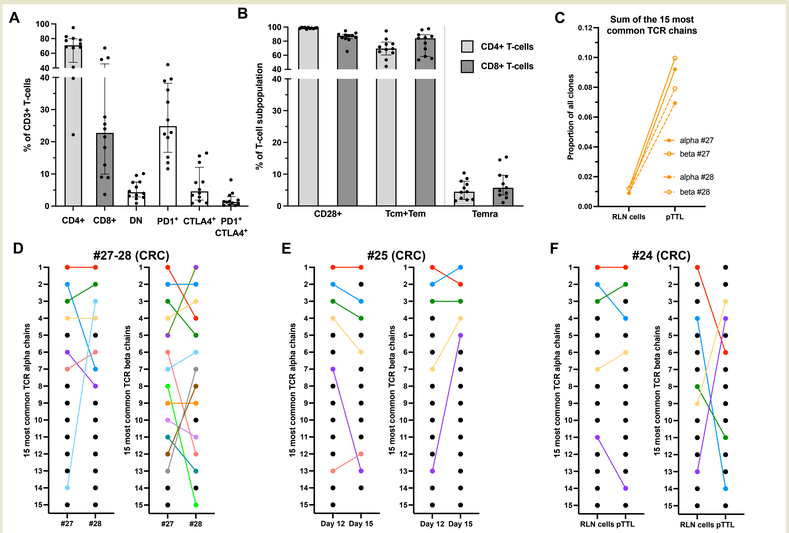
pTTL characterisation of n=12 development batches derived from urinary bladder cancer (UBC) or colorectal cancer (CRC) is presented.

pTTL identity

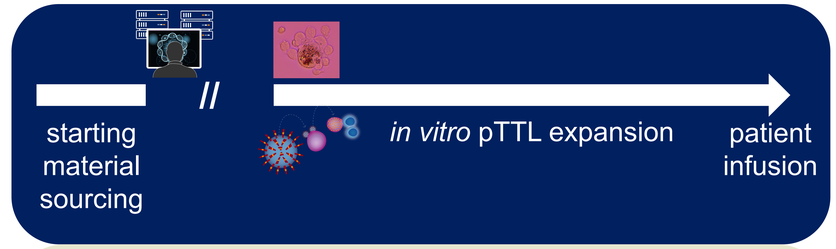
- Patient's individual variation confers pTTL's phenotypic diversity ($CD4^+$ and $CD8^+$ T-cells).

- pTTLs are mainly composed of Tcm or Tem cells. Only a small proportion display a phenotype indicative of a limited *in vivo* functionality.

- pTTLs are oligoclonal and partly derive from clones enriched in the starting material.

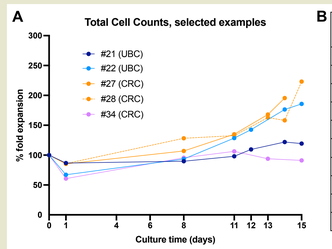


Flow cytometry analysis of $CD3^+$ T-cells (A) or T-cells subpopulations (B). DN: $CD3^+CD4^-CD8^-$ T-cells, Tcm+Tem: $CD45RA^-CCR7^{+/-}$, Temra: $CD45RA^+CCR7^-$. Enrichment (C) and conservation (D) of the 15 most common TCR chains in pTTLs derived from the same material (#27-28) by TCRseq.
(E) Conservation of the 15 most common TCR chains in pTTLs harvested on different culture days.
(F) Conservation of the 15 most common TCR chains between RLN cells and pTTLs.

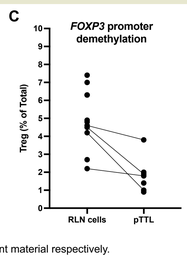


Expansion data

- Patient's individual variations confer growth kinetic diversity.
- pTTLs derived from UBC or CRC patient materials show comparability.
- EpiTCer® bead stimulation does not favour regulatory T cell expansion.



B	
Batch #	Production yield (seeded d0 vs formulated)
#21 (UBC)	87%
#22 (UBC)	156%
#24 (CRC)	99%
#25 (CRC)	38%
#26 (UBC)	94%
#27-28 (CRC)	143%-152%
#30 (CRC)	114%
#31-32 (CRC)	30%-83%
#33 (CRC)	251%
#34 (CRC)	92%



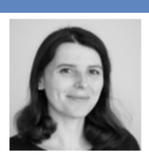
#27-28 and #31-32 pTTL derived from same patient material respectively.

(A) Selected examples of pTTL culture growth kinetics. (B) Summary of obtained production yields. (C) Proportion of regulatory T cells before (RLN cells) and after culture (pTTLs).

A First-in-human trial is underway

- Up to 16 adult patients with colorectal cancer Stage IV
- **Primary endpoint** - Safety
- **Secondary endpoints** - Standard clinical measurements: Response, OS, PFS, Disease-specific survival, Time to progression.
- **Exploratory endpoints** – *in vivo* characterisation: pTTL penetration, persistence, specificity and efficacy. Correlation between clinical outcome and neoantigen selection.

Anne-Laure JOLY, Ph.D.
Scientific Lead Cell Group
E-mail: anne-laure.joly@neogap.se
Phone: +46 737 215 912



NEOGAP Therapeutics AB
Visiting address: Visionsgatan 18II
171 64 Solna, Sweden
www.neogap.se