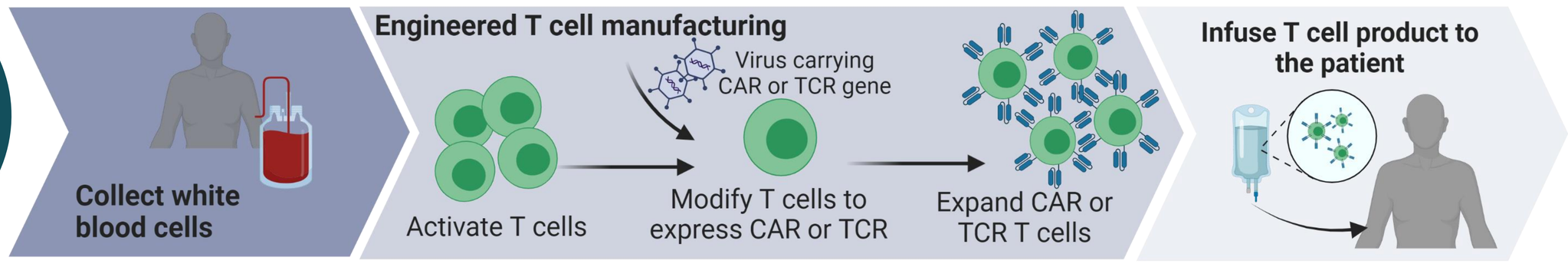
# CellFit: T-cells fit to fight cancer

Léa Rosselle[1], Fatemeh Kaveh[1], Hanne Haslene-Hox[2], Hanne Hein Trøen[2], Maxi-Lu Böschen[3], Tuva Holt Hereng[3], Evan Zynda[3], Sébastien Wälchli[1], Else Marit Inderberg[1].

**The use of T lymphocytes in adoptive cell therapy (ACT) shows great promise for treatment of cancers otherwise incurable. However, one of the largest challenges faced in cell-based cancer therapy is to provide an efficient and scalable production. The use of "living drugs" requires precise logistics at all stages of cell life: development, manufacturing, transport and finally the infusion to the patient. With the CellFit project, we aim to define optimal growth conditions for improved manufacturing of adapted therapeutic T cells required for solid tumor treatment.**

## ADOPTIVE CELL THERAPY AGAINST CANCER




## CURRENTLY

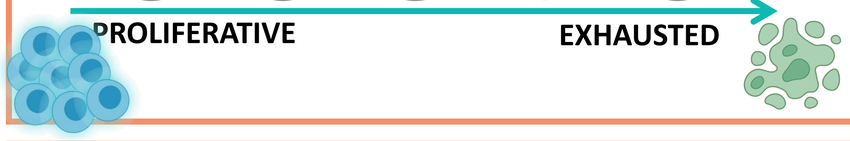
- Heterogeneous and exhausted population of T cells
- Lack of long-term persistence
- Loss of efficiency after injection

## HOW DO WE SOLVE THESE ISSUES ?

### STEM-CELL LIKE T CELL FOR A POWERFUL CULTURE

The stem cell state has been studied for many years for their higher potential to self renew in many tissue. In the case of T cell, Stem cell memory T cells ($T_{scm}$) are able to differentiate into T-cell central memory ($T_{cm}$) and T-cell effector memory ($T_{em}$) and show low signs of exhaustion. This cell subset is a good candidate for improving T-cell therapy but is present in very low numbers in T-cell culture. To be able to produce T cells of young/memory phenotype, a controlled T-cell activation process is needed. Many different serum sources, cytokines and growth factors or chemicals as well as stimulation can be explored to get an optimal T-cell culture.

#### T-CELL HETEROGENEITY

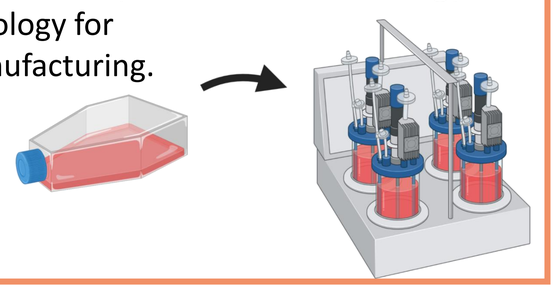



### INNOVATIVE REAGENT DEVELOPMENT

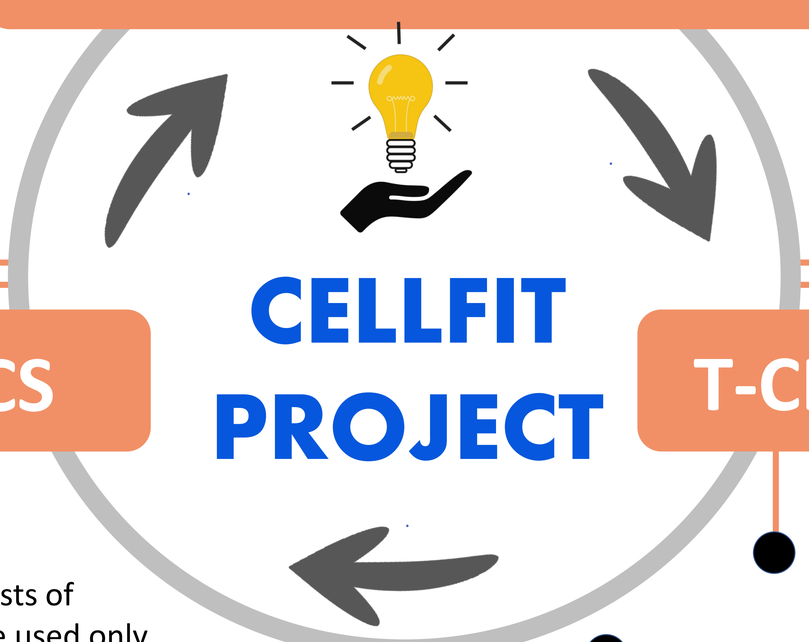
The design of new media and Dynabeads for T-cell expansion according to clinical grade cell culture exigencies is a key part of the optimisation of T-cell manufacturing.

### LARGE SCALE AND AUTOMATED CULTURE

After optimal culture selection, we will be able to establish a novel manufacturing method adapted to large-scale cGMP production and thus provide novel production methodology and technology for T-cell manufacturing.



## CULTURE OPTIMISATION

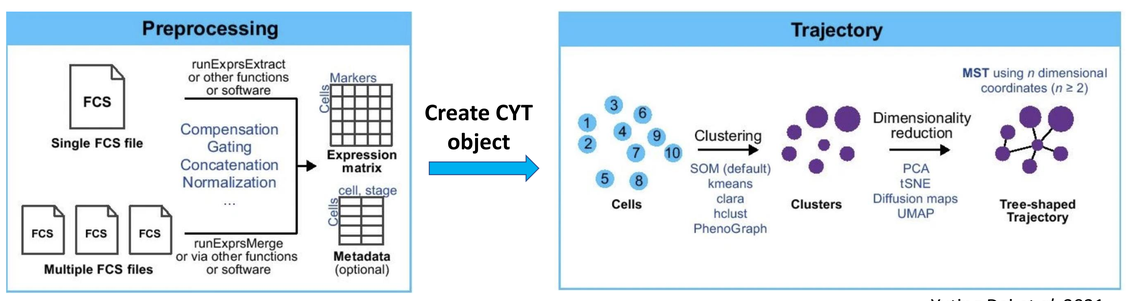


## CELLFIT PROJECT

## BIOINFORMATICS

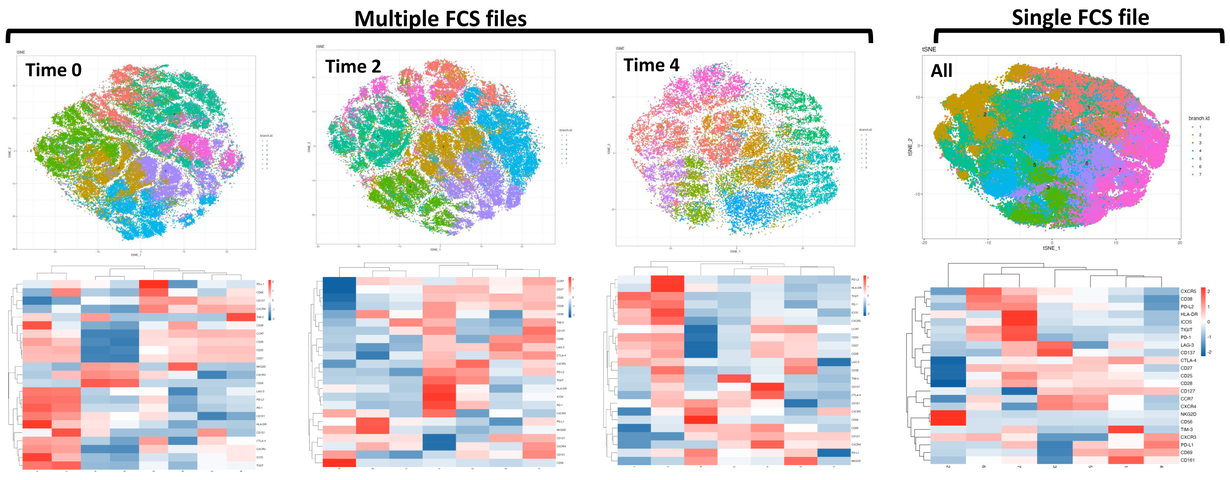
### PIPELINE

The bioinformatics pipeline for mass cytometry data consists of below R-packages: **Pre-processing:** CATALYST which will be used only for concatenations of truncated fcs.files and quality control. **Analysis:** will be done through CytoTree & FlowSOM packages. We will test 5 types of clustering methods through CytoTree and compare results to the commonly used Cytobank.



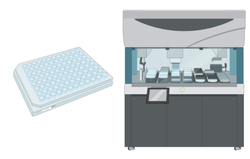

Yuting Dai *et al*, 2021

**Patient comparison:** Analysis of blood within 3 time points (0, 2, 4 months & all together) from a breast cancer patient treated with two different drugs.



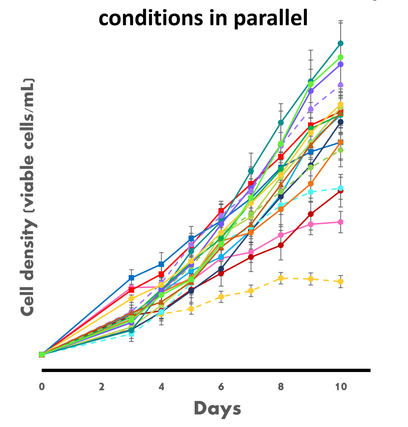

## T-CELL POPULATION STUDY

### HIGH THROUGHPUT SCREENING

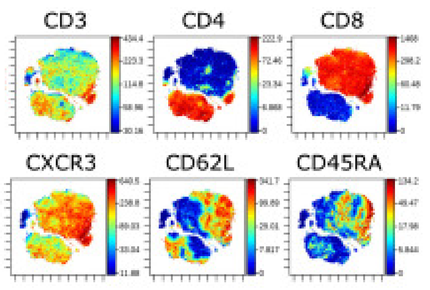


The set-up of T-cell expansion in 96-well plate format allow the extensive screening of culture conditions. The T-cell culture methods will be translated from manual to robotic set-ups where all pipetting, cell culturing and assay read-outs will be performed automatically with robots coupled to incubators, spectrophotometer and high-content confocal microscope.

**T-cell growth under different cultivation conditions can be tested with many conditions in parallel**

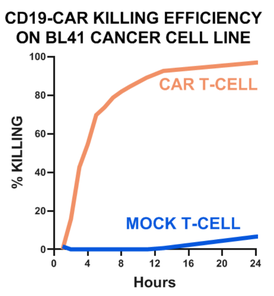



### FLOW AND MASS CYTOMETRY

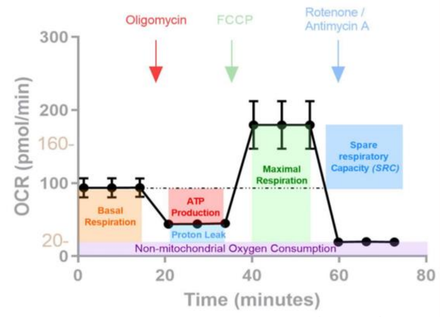



Dillard *et al*, 2021

### FUNCTIONAL ASSAYS




### METABOLIC ANALYSIS




Forcados *et al*, 2022

**Evaluate phenotype and metabolism of cellular subsets as well as therapeutic effect of produced cells.**

**Contact**

[1] Translational Research Unit, Section for Cellular Therapy, Department of Oncology, Oslo University Hospital-Radiumhospitalet, Oslo, Norway
[2] SINTEF Industry, Department of Biotechnology and Nanomedicine, Trondheim, Norway
[3] Cellular Medicine, Research and Development, Thermo Fisher Scientific, Oslo, Norway

Presenting author contact details: lea.rosselle@rr-research.no

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