



財團法人生物技術開發中心
Development Center for Biotechnology

Process Development of T Cells and Chimeric Antigen Receptor (CAR)-T Cells

Development Center for Biotechnology

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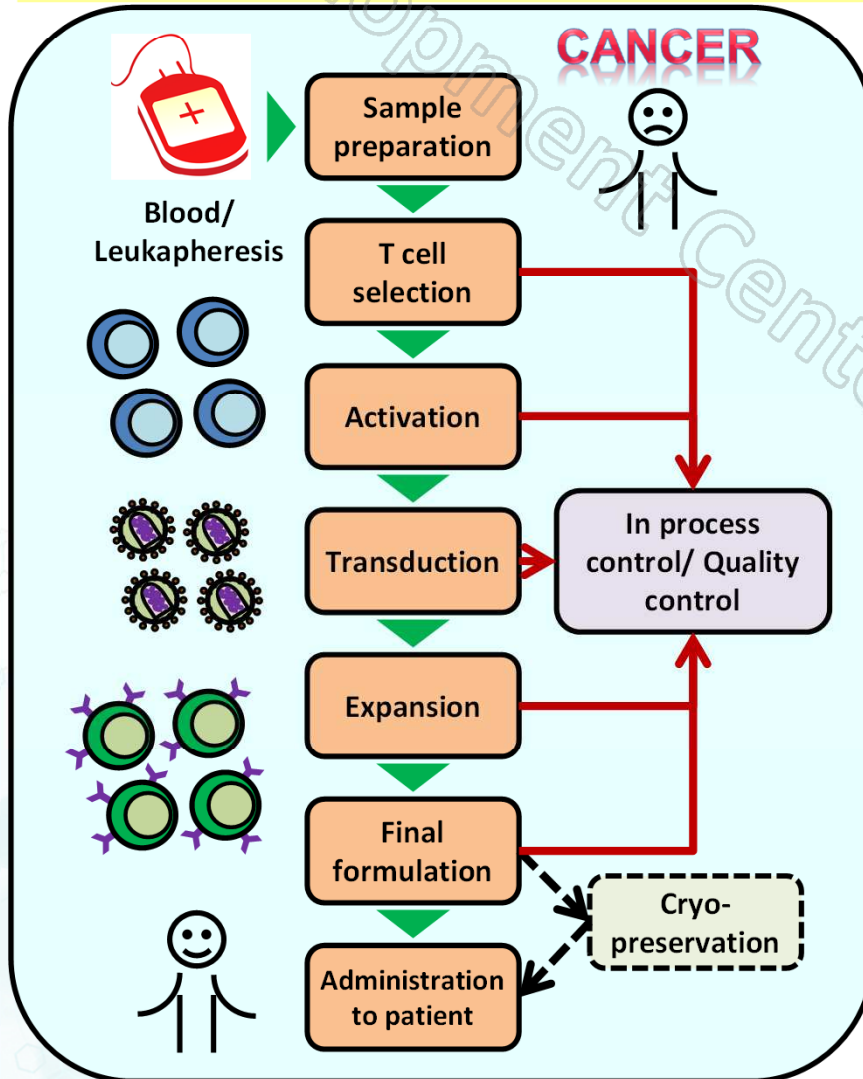
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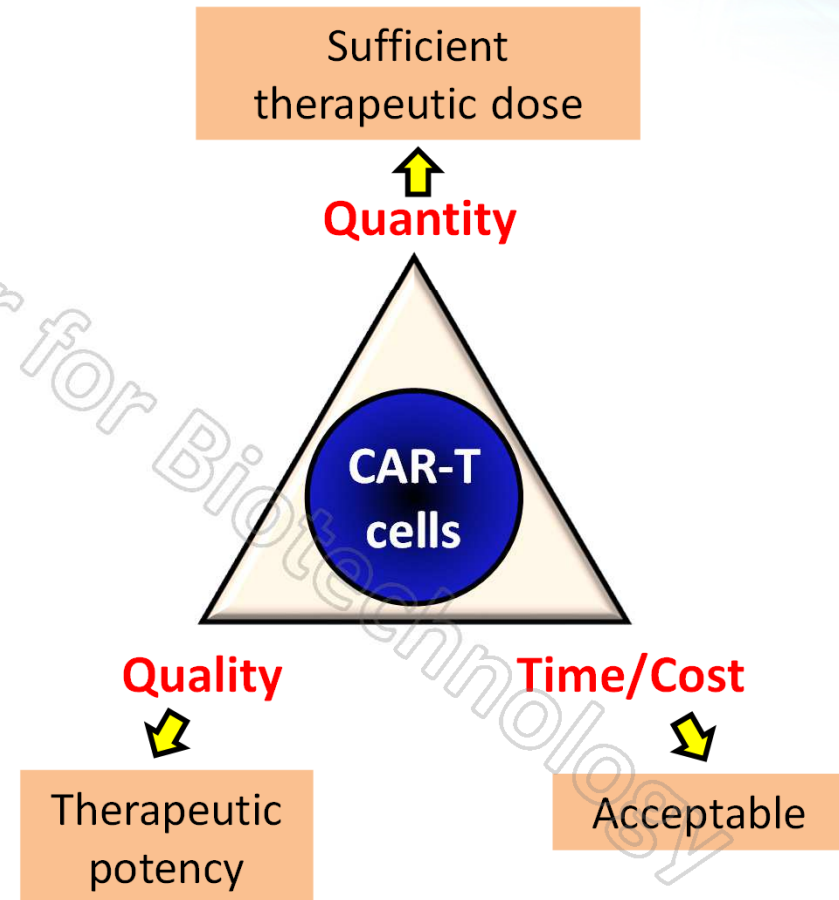


Bioprocess Development of CAR-T Cells

Complex Process of CAR-T Cells



Challenges of Process for Preparing CAR-T Cells

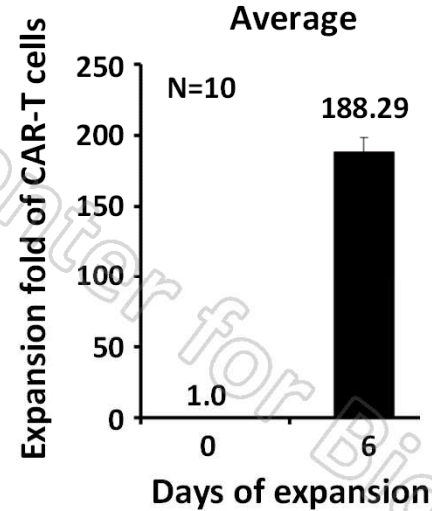
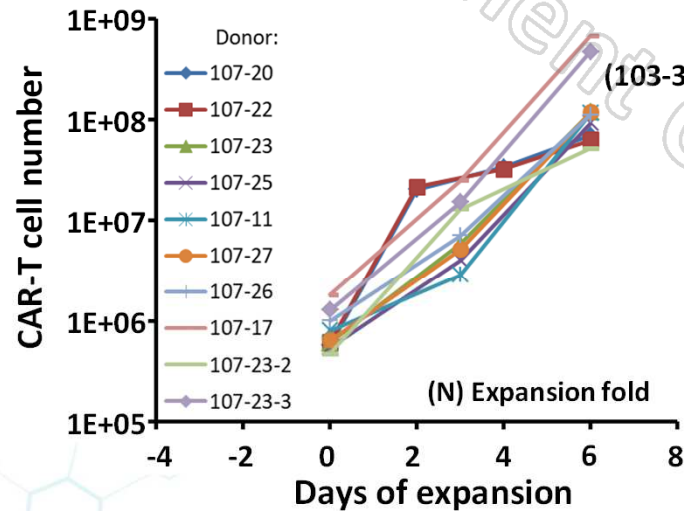


The Growth and Population of anti-CD19 CAR-T Cells were Consistent in DCB's Condition

Quantity

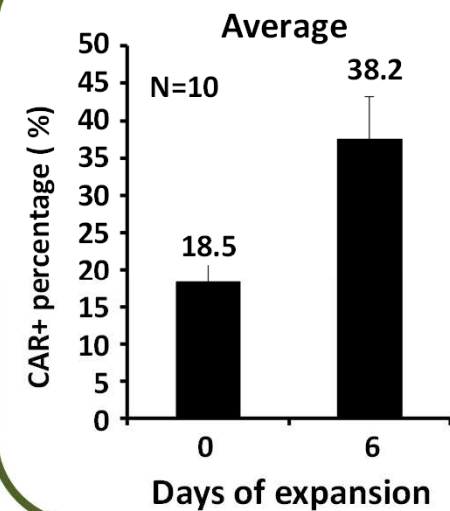
CAR-T cell number

Initial total T cell number: $\sim 1 \times 10^6$ total T cells



CD19 CAR-T cells (N=10)

CAR+ percentage

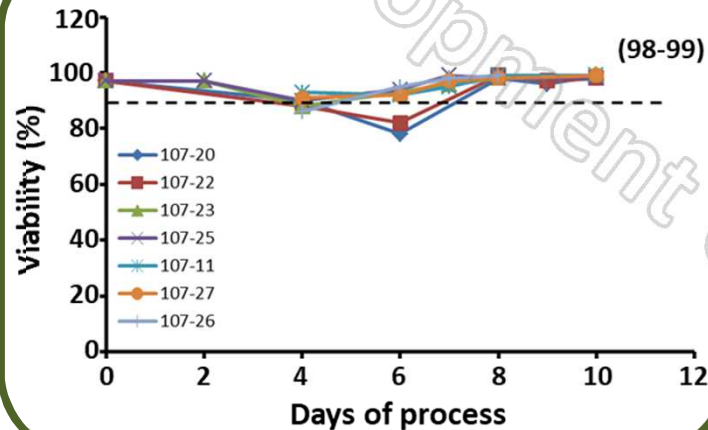


- Anti-CD19 CAR-T cells expanded to averagely about **188** fold in a **6 day-culture**.
- **CAR+** population was increased averagely **20%** as compared to initial population.

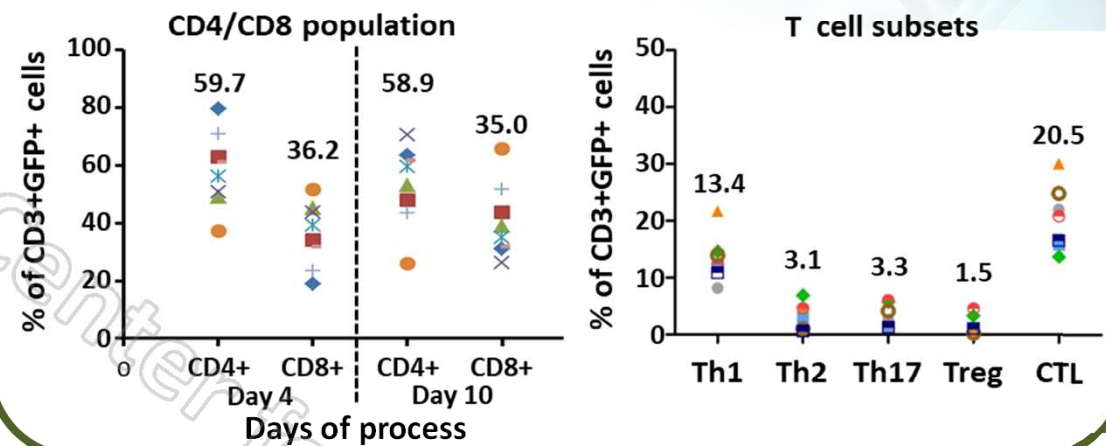
Maintained CD4+ and CD8+ T Cells at High Viability and with Stem Cell Memory T Cell stage

Quality

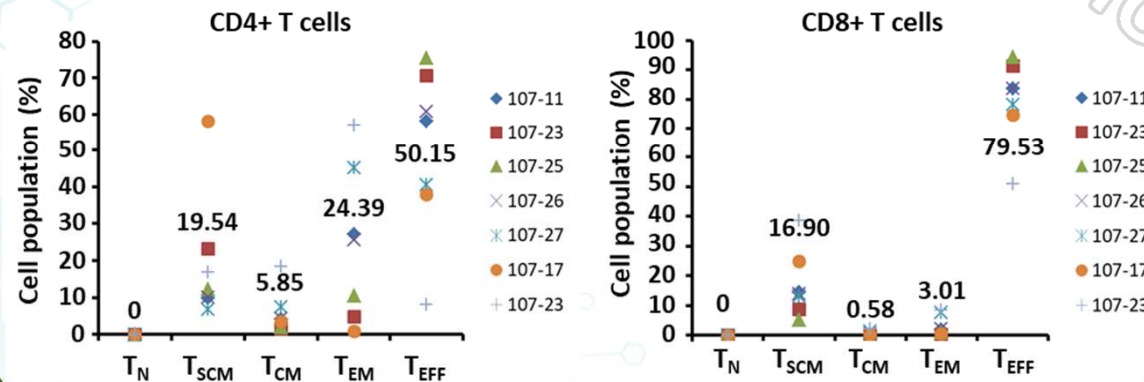
Cell viability



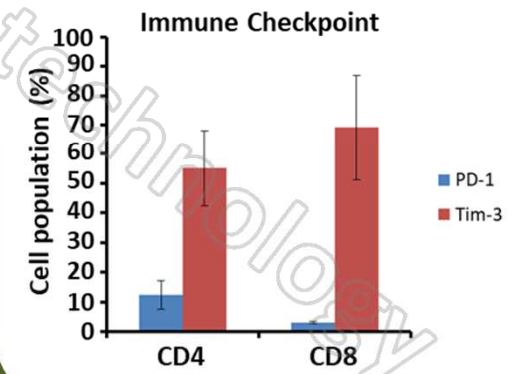
T cell population



T cell differentiation stage



Immune checkpoint



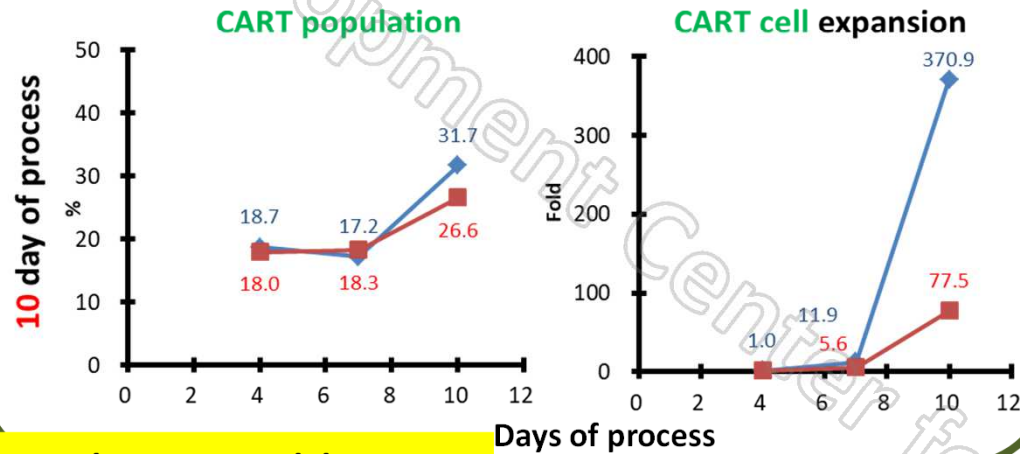
T_N: Naive T cells; T_{SCM}: Stem cell memory; T_{CM}: Central memory; T_{EM}: Effector memory; T_{EFF}: Effector T cells

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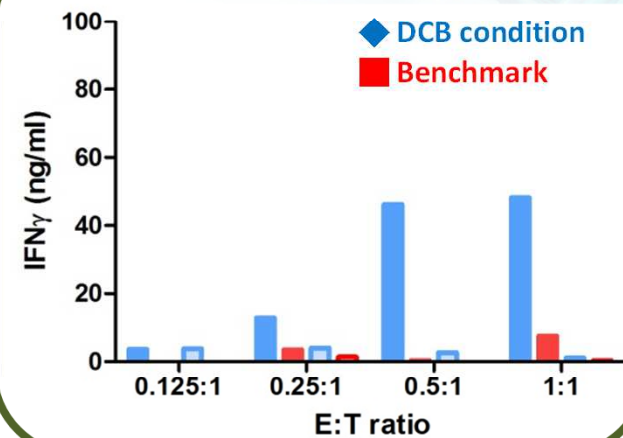
The Expansion and Response of CAR-T Cells in DCB Condition were Higher than Benchmark

Quality

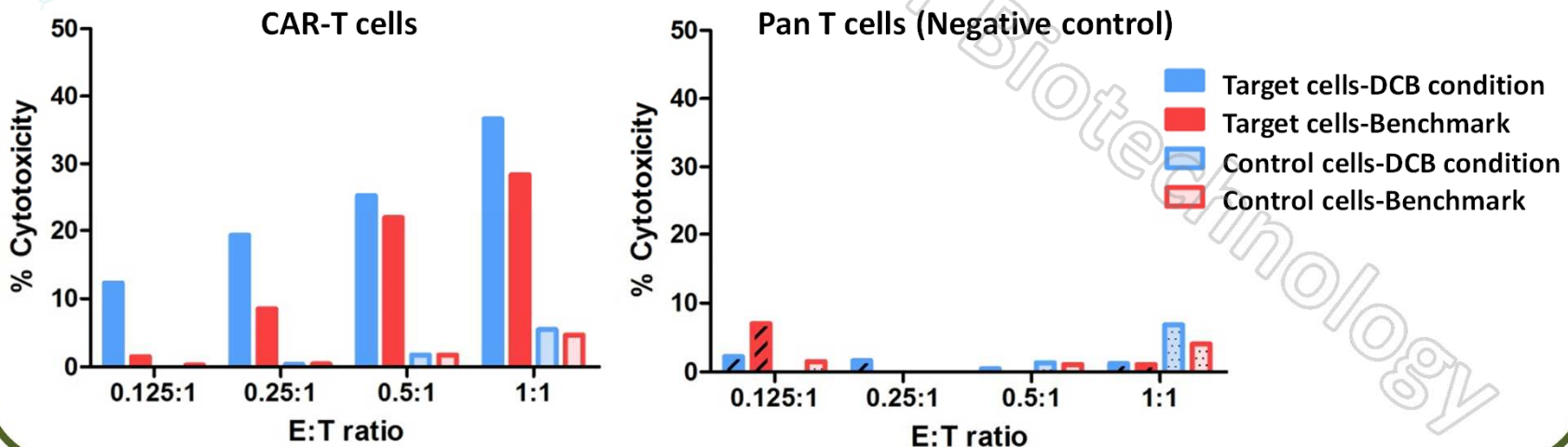
CAR-T Cell population and Expansion



Cytokine production assay

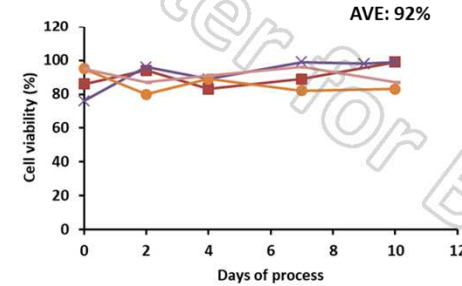
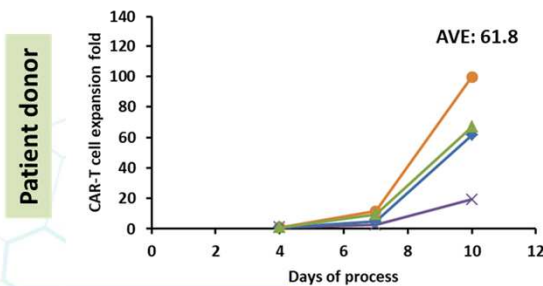
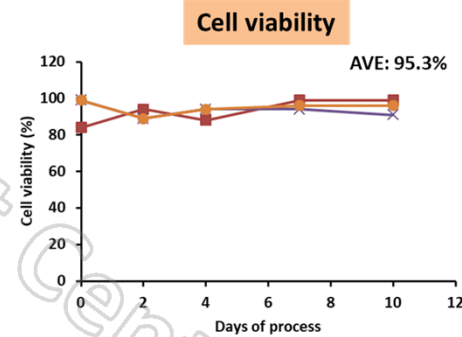
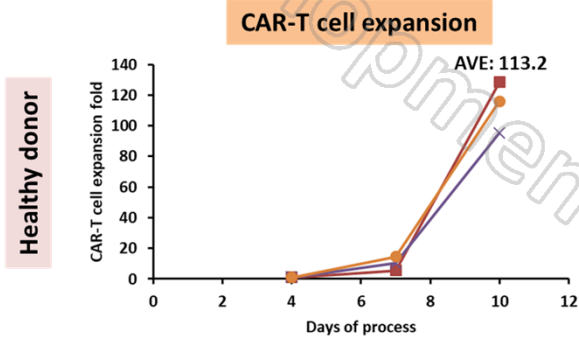


In Vitro cytotoxicity assay

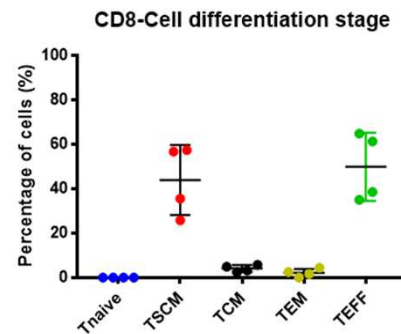
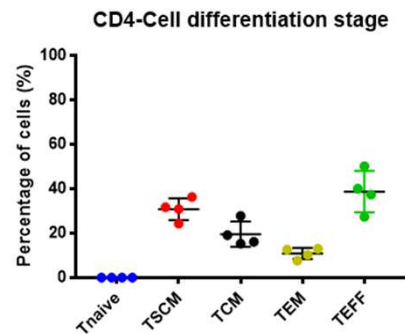
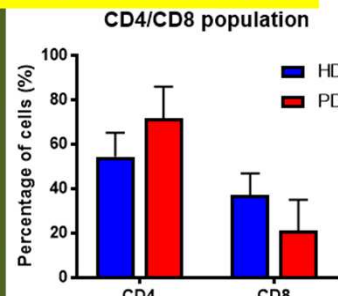


CAR-T Cells Derived from Cancer Patients and Healthy Donors Showed Comparable Potency

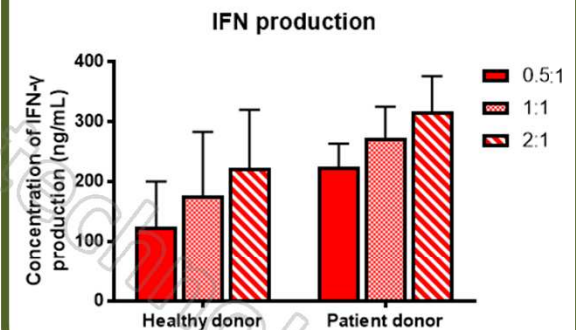
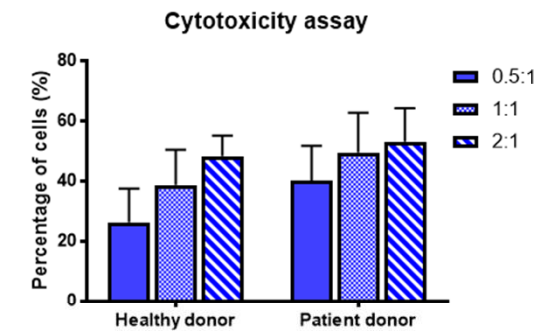
Growth of CAR-T cells



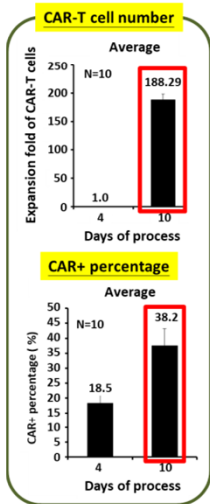
CAR-T cell subsets



In Vitro CAR-T cell activity

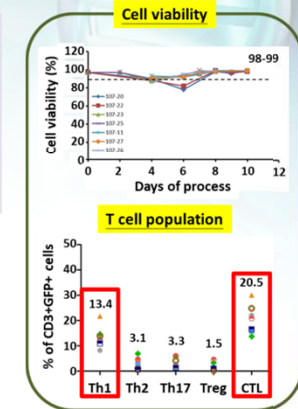


Summary of CAR-T Cell Bioprocess in DCB



- **High cell expansion fold:**
Expanding averagely **93-188 fold** in **6 day**-expansion.
- **Increase CAR+ cell population:**
Increasing **5-20%** of CAR+ cells

- **High cell viability:**
Above **98%** at the endpoint
- **Cellular immunity populations:**
Th1 and **CTL** were major subsets



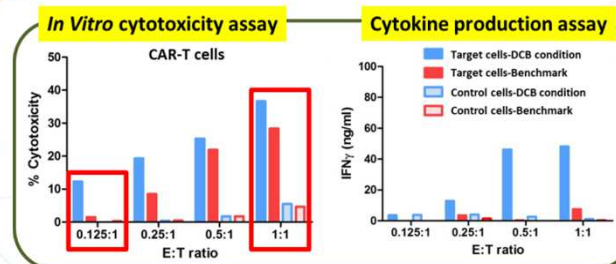
Quantity

Potency

Quality

Wide application

- **Higher cytotoxicity activity:**
Increasing **5-10%** of target cell killing
- **Higher cytokine production:**
Increasing **5-30 ng/mL** of IFN- γ production *in vitro*



- **Simple generic conditions:**
3 CAR-T cells have been applied in the optimized conditions.