RegMedNet | Spotlight

CellGenix

Introducing CellGenix® T Cell Medium – early onset of T cell expansion for faster T cell therapy manufacturing

Achieve an early onset of T cell expansion and sustained viability with the novel CellGenix® (Freiburg im Breisgau, Germany) T Cell Medium (CellGenix® TCM).

Serum-free T cell therapy manufacturing

CellGenix® (Freiburg im Breisgau, Germany) T Cell Medium (CellGenix® TCM) offers a serum-free and xeno-free alternative for rapid expansion of functional human T cells. Due to stable glutamine in the formulation it is ready-to-use for T cell cultures without the need for supplementation with human serum or glutamine. Many current T cell therapy protocols rely on the addition of human serum.

Eliminating the use of human serum will reduce the failure rate in your manufacturing process due to the high lot-to-lot inconsistencies of serum. Since human serum is a limited resource and might not be available in large quantities it is unsuitable for commercial scale manufacturing. Furthermore, the human origin of serum poses a certain risk of containing adventitious agents and therefore does not meet global regulatory guidelines.

Early onset of T cell expansion and sustained viability

T cell culture in CellGenix® TCM results in high cell numbers early after activation and throughout cell culture with high viability. This early onset of T cell expansion allows for faster T cell therapy manufacturing, which can significantly reduce your cost of goods.

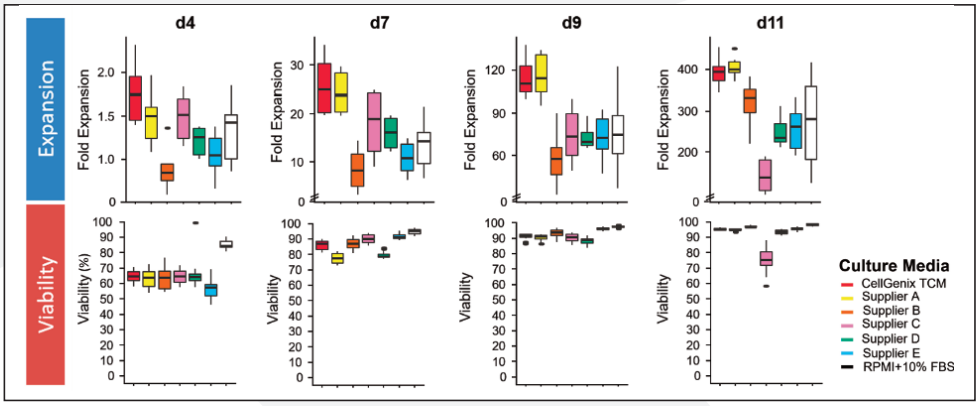

Figure 1: Fold T cell expansion and cell viability on the indicated day of culture: CD3+ T cells were activated with anti-CD3/anti-CD28-coupled beads and cultivated in CellGenix® TCM or competitor media in the presence of IL-7 and IL-15 (10 ng/ml, CellGenix). On the indicated day cells were labeled with 7-AAD and viability was determined by flow cytometry. Median and spread of n=6 donors are displayed for expansion (upper panels) and cell viability (lower panels).

Promotion of a central memory and early differentiated memory T cell phenotype

During T cell culture in CellGenix® TCM a 'young' phenotype of naïve T cells/memory stem T cells ($T_{N/SCM}$ cells) or central memory T cells (T_{CM} cells) is acquired. These phenotypes represent the most undifferentiated memory T cell phenotypes, meaning that they have the highest proliferation potential, self-renewal properties and longer survival rates.

It has been shown that the engraftment and persistence of T cell products in patients is associated with a T_{CM} phenotype, rather than more differentiated memory phenotypes [1]. T_{SCM} are considered as even less differentiated cells with potentially even better persistence. It has been reported that for CD19 CAR-T cells the expansion of patient-infused cells is correlated with the frequency of $CD8^+$ T_{SCM}-like cells [2]. It is therefore beneficial for your T cell therapy product to obtain a central memory and early differentiated memory T cell phenotype.

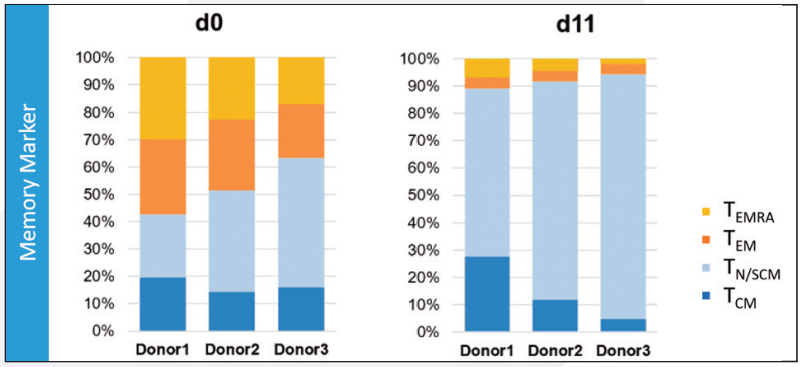

Figure 2: Memory phenotype of starting population and after expansion in CellGenix® TCM: CD3+ T cells were activated with anti-CD3/anti-CD28-coupled beads and cultivated in CellGenix® TCM or competitor media, in the presence of interleukin (IL)-7 and IL-15 (10 ng/ml, CellGenix). On day 0 (left panel) and day 11 (right panel) the expression of memory cell markers was determined by flow cytometry for three donors. TCM, central memory T cells; TN, naïve T cells; TSCM, memory stem T cells; TEM, effector memory T cells; TEMRA, terminally differentiated effector T cells.

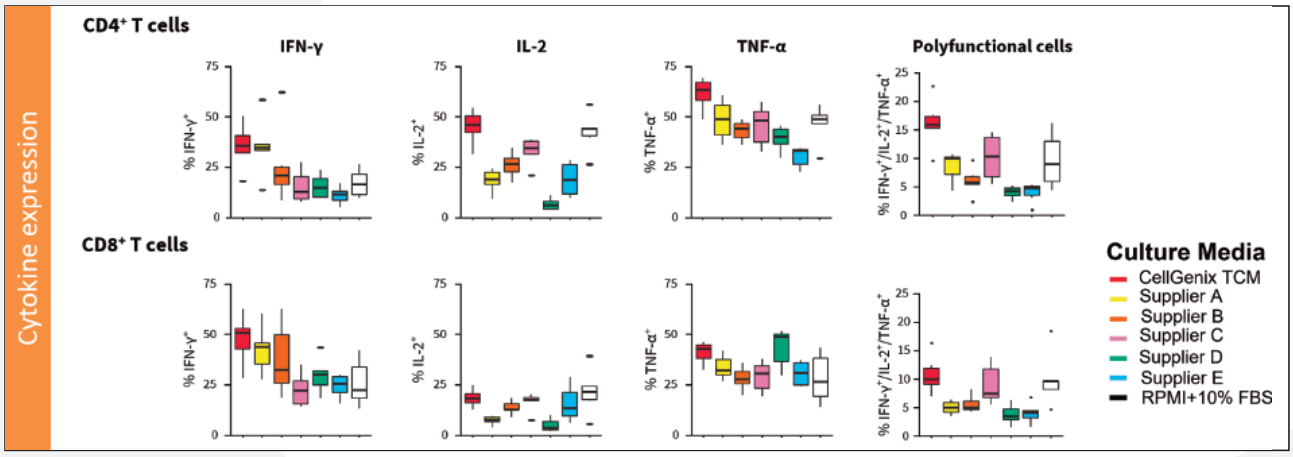

Figure 3: Cytokine expression after expansion in CellGenix® TCM: CD3+ T cells were activated with anti-CD3/anti-CD28-coupled beads and cultivated in CellGenix® TCM or competitor media in the presence of IL-7 and IL-15 (10 ng/ml, CellGenix). On day 11 of culture, cells were re-stimulated using phorbol 12-myristate 13-acetate (PMA) and Ionomycin in the presence of brefeldin A. Cells were fixed and permeabilized and the expression of the indicated cytokines was determined by flow cytometry. Median and spread of n=6 donors are displayed for CD4+ (upper panels) and CD8+ (lower panels), black dots indicate statistical outliers.

High proportion of cytokine producing cells including polyfunctional cells

An important aspect of T cell functionality is the secretion of cytokines such as interleukin-2 (IL-2), interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α). After cultivation in CellGenix® TCM a high proportion of cytokine producing cells is obtained including polyfunctional cells (expressing more than one cytokine).

A recent report suggests that the combination of cell frequency and cytokine production levels of polyfunctional CD19 CAR-T cells is correlated with the clinical outcome in patients with non-Hodgkin lymphoma [3]. Obtaining cytokine secreting T cells, in particular polyfunctional cells, could therefore have a positive effect on the therapeutic response of your T cell therapy product.

1. Schmueck-Henneresse M, Omer B, Shum T et al. Comprehensive approach for identifying the T cell subset origin of CD3 and CD28 antibody–activated chimeric antigen receptor–modified T cells. J Immunol. 199(1), 348–362 (2017).
2. Xu Y, Zhang M, Ramos C et al. Closely related T-memory stem cells correlate with in vivo expansion of CAR.CD19-T cells and are preserved by IL-7 and IL-15. Blood. 123(24), 3750–3759 (2014).
3. Rossi J, Paczkowski P, Shen Y et al. Preinfusion polyfunctional anti-CD19 chimeric antigen receptor T cells are associated with clinical outcomes in NHL. Blood. 132(8), 804–814 (2018).

CellGenix is a leading global supplier of high-quality raw materials for the expanding cell and gene therapy and regenerative medicine space. We develop, manufacture and market human cytokines and growth factors, in preclinical and GMP quality, along with GMP serum-free media for further manufacturing of advanced therapeutic medical products. With more than 25 years of experience we are experts in the GMP manufacturing of raw materials for the cell and gene therapy space. As a former advanced therapeutic medical products developer and manufacturer we gained in-depth cell culture knowledge and superior regulatory expertise. With this unique background we understand the high requirements our customers face during product development and the regulatory approval process. By offering expert technical and regulatory support we can help simplify raw material qualification and validation efforts.

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