Improved COGs with nLiven PR®

Preserving the promise™

nLiven PR®– BioDefined Media supports reduced cytokine supplementation for T cell expansion.

The challenge

Chimeric Antigen Receptor T cell (CAR-T) therapies have shown incredible efficacy against multiple hematological cancers. At present, the majority of both commercially available products and those in clinical trials are autologous by nature. Given the inherent variability of these starting materials, manufacturing processes strive to limit variability from other process inputs such as cell culture reagents. We have previously described how BioDefined Media can provide a more standardized alternative to human AB Serum (ABS),[1,2] whilst also inferring a preferential Tn/Tcm phenotype with improved efficacy in vivo[3]. Herein, we would like to describe how the composition of BioDefined Media allows for reduction in cytokine supplementation and reduced overall cost of goods (COGs).

Under the conditions of our study, replacement of ABS with nLiven PR results in a reduced need for IL2 in a CAR-T manufacturing process with a projected cost improvement of ~$3M over 10,000 patient doses. These savings could potentially allow for employment of an additional 40FTEs dedicated to manufacturing. Combined with the positive impact on T cell expansion and phenotype, nLiven PR is quickly establishing itself as the gold standard supplement for CAR-T manufacturing.

Unique protein profile of hPL

Cytokines represent a significant component in the COGs model of cell therapies due to both the high cost of GMP reagents and the cost of qualifying new materials due to variability. Simplifying the manufacturing process by removing variable and expensive components will result in not only lower overall costs, but also reduced risks in manufacturing a reproducible product. We previously introduced the concept of BioDefined media[1] and referenced some of the work undertaken to characterize the composition of our nLiven PR, an irradiated human platelet lysate (hPL), compared with ABS. While a component of platelet lysate is certainly similar to serum, there is a very distinct composition, as demonstrated by analyzing the distribution of proteins.

Figure 1: Proteomic volcano plot of proteins in nLiven PR and ABS.

In addition to the data presented in that paper, the proteomic data revealed significantly higher values of T cell expansion-associated cytokines IL-2, IL-7, and IL-15 (Table 1). This observation suggested that the composition of nLiven PR could reduce the need for additive interleukin addition.

IL	nLiven PR pg/mL (SD)	ABS pg/mL (SD)
IL 2	67 (9)	1 (1)
IL 7	322 (24)	4 (7)
IL 15	44 (9)	18 (17)

Table 1: RayBioTech Assay data for nLiven PR (3 lots) and ABS (3 lots).

Our goal

We looked as to whether supplementing T cell cultures with nLiven PR in place of ABS could allow for lower concentrations of cytokines to be added. The results of the study showed that nLiven PR does support the reduction of supplemental cytokine addition. In the case of IL 2, use of nLiven PR and IL 2 at 50 IU/mL resulted in the same expansion as ABS and 100 IU/mL IL 2.

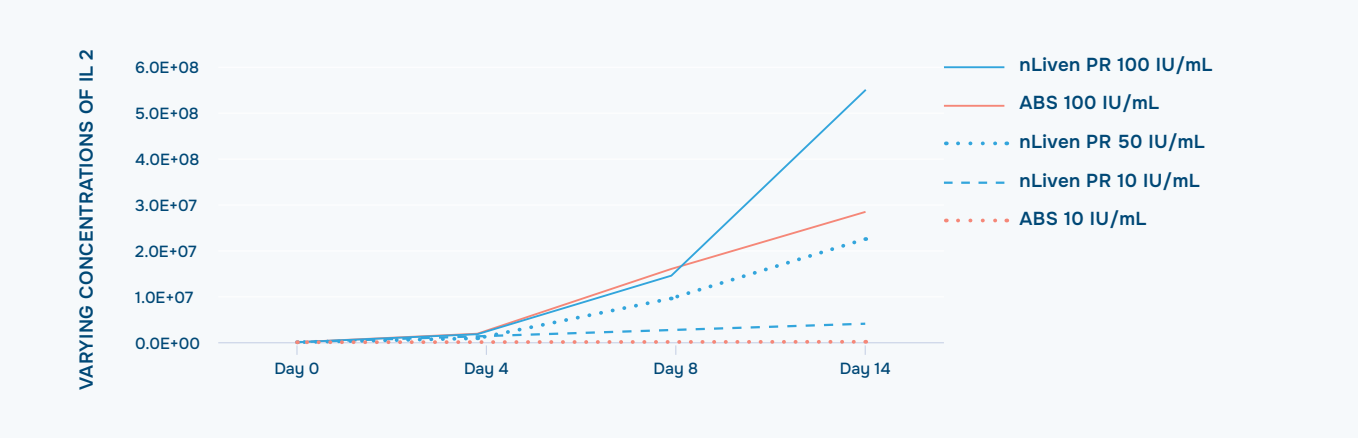

Figure 2: T cells growth in nLiven PR or ABS with varying concentrations of IL7/IL15 or IL2.

Impact

Interleukins such as IL-2, IL-7, and IL-15 represent a significant contributor of cell therapy manufacturing COGs. This study demonstrated the ability to reduce IL-2 concentrations by 50% when supplementing the culture medium with nLiven PR versus ABS. This reduction in raw material costs could be substantial at scale, allowing for reallocation of resources, reduced manufacturing costs, and potentially reduced drug costs.

References

1. Sexton Biotechnologies (now part of BioLife Solutions). Redefining Cell Culture Supplementation. Phacilitate, (2021).
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3. Torres Chavez, A., McKenna, M.K., Canestrari, E. et al. Expanding CAR T cells in human platelet lysate renders T cells with in vivo longevity. *Journal for ImmunoTherapy Cancer* 7, 330 (2019). https://doi.org/10.1186/s40425-019-0804-9

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