DEVELOPMENT OF A CHEMICALLY DEFINED, ANIMAL-COMPONENT-FREE EX VIVO EXPANSION PROCESS FOR ACTIVATED HUMAN T CELLS

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T-cell based immunotherapy applications have recently drawn great interest and notoriety due to their clinical potential as next-generation life-saving therapies for cancer patients. Generation of sufficient, desired T-cell populations is an essential task for the successful development of T-cell based immunotherapy, requiring an effective, scalable, and consistent ex vivo manufacturing process. A suitable chemically-defined (CD), animal-component-free (ACF) T-cell basal medium would significantly foster the establishment of such a process. Presented in this study is the development of a CD, ACF T-cell basal culture medium that is scalable and suitable for the manufacture of adoptive T-cell therapy products. A 'quality of design' approach coupled with spent media analysis was utilized to examine the effects of various key media compositions such as amino acids, vitamins, minerals, and lipids on activated human peripheral blood-derived T cells proliferation. The resulting CD, ACF basal expansion medium was comparable or superior to media containing serum (RPMI + 10% FBS) or serum-derived human albumin in the culture of both CD4+ and CD8+ T-cell populations. Further supplementation with proper cytokine combinations verified and demonstrated the CD, ACF basal media's performance in effectively supporting the derivation of major T helper subsets, such as Th1, Th2 and Treg, from naïve CD4+ T cells. In addition to its utility in static culture conditions using T-flasks, the CD, ACF basal medium was subsequently evaluated for its potential application in other commonly used expansion vehicles including spinner flasks, culture bags, and G-Rex plate systems. A total expansion of 50 and 80-fold was achieved through the G-Rex plate and culture bag systems, respectively, when cultures were maintained for up to 14 days accompanied by a single media replenishment event suggesting the potential for even higher yields with further optimization and feeding steps. In all cases, the CD, ACF medium delivered the best growth profile while maintaining high viability and desired T-cell phenotypes (e.g. % of CD62L+ cells). The evaluation results demonstrate the improved performance delivered by the CD, ACF medium over serum-containing media and its suitability for use in the manufacture of adoptive T-cell therapy products.