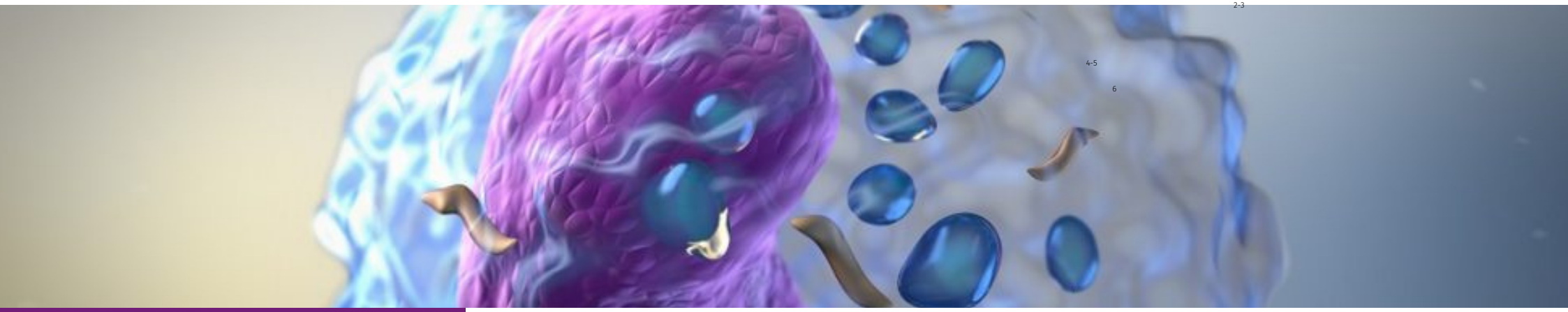
OrganaBio

CASE STUDY



Rapid curation of a robust, recallable donor pool of CMV seropositive donors for delivery of RUO and GMP LeukoPACs™ to an international CDMO

INTRODUCTION

The monoclonal antibodies (mAbs) daratumumab, and elotuzumab have been approved by the US Food and Drug Administration for treating multiple myeloma (MM) in 2015. Although clinical responses have been promising, most patients' disease eventually progresses [1]. One of the potential anti-tumor mechanisms of mAbs in MM patients is antibody-dependent cellular cytotoxicity (ADCC) which is mediated by natural killer (NK) cells. NK cells are activated when the Fc portion of an antibody (bound to target tumor cell) binds their Fc receptor (FcγRIIIa or CD16a) and triggers activation, degranulation, and tumor killing [2-3].

In efforts to enhance ADCC and tumor killing, researchers have identified a novel, relatively rare subset of human NK cells with increased ADCC activity following NK Fc receptor crosslinking [4-5]. This special NK cell subset is only detectable at levels of 3 - 10% of total NK cells in only 25 - 30% of cytomegalovirus (CMV) seropositive individuals [6]. In order to utilize this specific NK cell subset as potential MM therapy, our client has developed an expansion method to allow scale up and manufacturing of these unique NK cells as an off-the-shelf, allogeneic cell therapy. To obtain these NK cells, our client needed a robust supply of fresh leukopaks from CMV seropositive donors.

OrganaBio was able to meet the client's unique needs to rapidly provide PBMCs from 100 CMV+ donors for screening and donor qualification, to subsequently draw RUO and GMP LeukoPACs from selected donors, and to ship fresh leukopaks to the client's CDMO in Singapore.

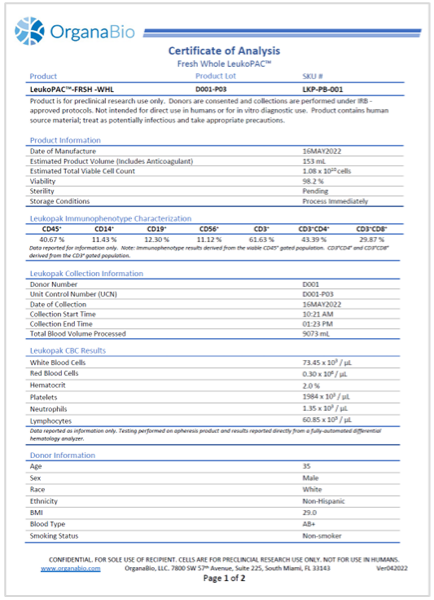
PROJECT OVERVIEW

The client reached out to OrganaBio about a multi-phase project pertaining to extensive CMV seropositive donor screening for IND (investigational new drug) application-enabling work. For the initial phases of the project, the client required PBMC vials from leukapheresis of 100 unique CMV seropositive donors for testing. Later phases of the project included collections of whole fresh RUO and GMP leukopaks from donors identified to meet phenotypic and functional requirements of the client.

To rapidly screen donors while minimizing cost to the client, the OrganaBio team suggested whole blood draws from donors as opposed to full leukapheresis collections. The minimal blood draw allowed donors to return sooner for a full collection (due to an 8-week deferral period between leukapheresis procedures) and was a cost-effective way for the client to screen and select donors. Donor recruitment, screening, and sample collections were performed by OrganaBio's wholly-owned leukapheresis subsidiary, HemaCenter, LLC.

PROJECT MANAGEMENT

Utilizing our dedicated project manager, the project was managed cross-functionally by coordinating OrganaBio's Sales, Process Development, and Operations teams and HemaCenter staff, and timely updates were provided to the client via bi-weekly meetings to maintain clear, comprehensive, and timely communications. In addition, a project management software was regularly updated by the different departments at OrganaBio, and the client was able to follow project progress at any time, view all donor attributes and sample characteristics, and note which donors were critical to their process.



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Certificate of Analysis

Fresh Whole LeukoPAC™

Product	Product Lot	SKU #
LeukoPAC™-FRSH -WHL	D001-P03	LKP-PB-001

Product is for preclinical research use only. Donors are consented and collections are performed under IRB-approved protocols. Not intended for direct use in humans or for in vitro diagnostic use. Product contains human source material; treat as potentially infectious and take appropriate precautions.

Product Information

Date of Manufacture	16MAY2022
Estimated Product Volume (Includes Anticoagulant)	153 mL
Estimated Total Viable Cell Count	1.08×10^{10} cells
Viability	98.2 %
Sterility	Pending
Storage Conditions	Process Immediately

Leukopak Immunophenotype Characterization

CD45+	CD14+	CD19+	CD56+	CD3+	CD3+CD4+	CD3+CD8+
40.67 %	11.43 %	12.30 %	11.12 %	61.63 %	43.39 %	29.87 %

Data reported for information only. Note: Immunophenotype results derived from the viable CD45+ gated population. CD3+CD4+ and CD3+CD8+ derived from the CD3+ gated population.

Leukopak Collection Information

Donor Number	D001
Unit Control Number (UCN)	D001-P03
Date of Collection	16MAY2022
Collection Start Time	10:21 AM
Collection End Time	01:23 PM
Total Blood Volume Processed	9073 mL

Leukopak CBC Results

White Blood Cells	73.45×10^3 / µL
Red Blood Cells	0.30×10^6 / µL
Hematocrit	2.0 %
Platelets	1984×10^3 / µL
Neutrophils	1.35×10^3 / µL
Lymphocytes	60.85×10^3 / µL

Data reported as information only. Testing performed on apheresis product and results reported directly from a fully-automated differential hematology analyzer.

Donor Information

Age	35
Sex	Male
Race	White
Ethnicity	Non-Hispanic
BMI	29.0
Blood Type	AB+
Smoking Status	Non-smoker

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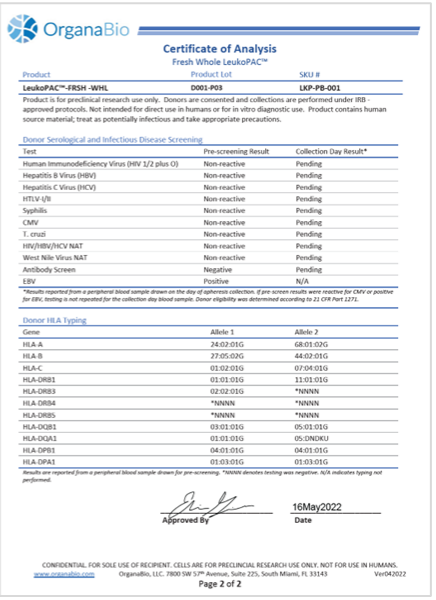

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Donor Serological and Infectious Disease Screening

Test	Pre-screening Result	Collection Day Result*
Human Immunodeficiency Virus (HIV 1/2 plus O)	Non-reactive	Pending
Hepatitis B Virus (HBV)	Non-reactive	Pending
Hepatitis C Virus (HCV)	Non-reactive	Pending
HTLV-I/II	Non-reactive	Pending
Syphilis	Non-reactive	Pending
CMV	Non-reactive	Pending
T. cruzi	Non-reactive	Pending
HIV/HBV/HCV NAT	Non-reactive	Pending
West Nile Virus NAT	Non-reactive	Pending
Antibody Screen	Negative	Pending
EBV	Positive	N/A

**Results reported from a peripheral blood sample drawn on the day of apheresis collection. If pre-screen results were reactive for CMV or positive for EBV, testing is not repeated for the collection day blood sample. Donor eligibility was determined according to 21 CFR Part 1271.*

Donor HLA Typing

Gene	Allele 1	Allele 2
HLA-A	24:02:01G	68:01:02G
HLA-B	27:05:02G	44:02:01G
HLA-C	01:02:01G	07:04:01G
HLA-DRB1	01:01:01G	11:01:01G
HLA-DRB3	02:02:01G	*NNNN
HLA-DRB4	*NNNN	*NNNN
HLA-DRB5	*NNNN	*NNNN
HLA-DQB1	03:01:01G	05:01:01G
HLA-DQA1	01:01:01G	05:ONDKU
HLA-DPB1	04:01:01G	04:01:01G
HLA-DPA1	01:03:01G	01:03:01G

*Results are reported from a peripheral blood sample drawn for pre-screening. *NNNN denotes testing was negative. N/A indicates typing not performed.*

Approved By 16May2022 Date

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Each LeukoPAC is accompanied by a comprehensive Certificate of Analysis (CoA). CoAs are included with all OrganaBio products, including tissues, blood, and isolated cells.

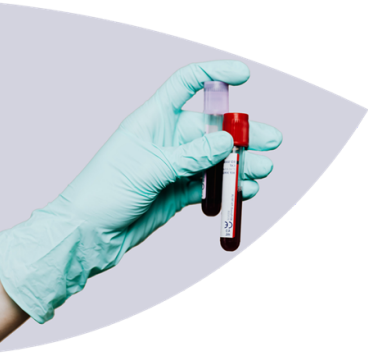
DONOR SCREENING, SELECTION, AND MANAGEMENT

PBMCs were isolated from whole blood samples using OrganaBio's standard protocol, and the client was provided with 5 million and 25 million PBMC vials from each donor. The 5 million PBMC vials were shipped directly to the client for their in-house screening, and the 25 million PBMC vials were shipped by OrganaBio to a third-party custom screening laboratory selected by the client. Sending vials directly to the third-party lab streamlined logistics for the client, which further reduced costs and accelerated timelines.

The client analyzed data from the screening tests to select donors who best fit their target patient profile. For donors with inconclusive testing results, OrganaBio was able to provide larger fill sizes of 100 million PBMCs for additional testing. Leveraging OrganaBio's donor pool, the client was able to identify suitable donors at a rate of 11.8% compared to a prior rate of only 5% when working with other vendors.

Using a critical donor list generated from the data from PBMC screening, OrganaBio was able to curate a donor pool specifically for the client and to secure primary and backup donors for each full leukopak collection to mitigate risk and ensure completed and on-time collections.

HemaCenter staff maintained a cadence for donor contact at regular intervals to ensure donors remained engaged, eligible (via coaching on lifestyle choices and preparation for donation), and recallable for the later phases of the project. At the time of publication of this report, donor recall rate from the curated donor pool was 100% for the duration of the project.



HEMACENTER

OrganaBio's wholly-owned apheresis collection subsidiary

Week 1				Week 12	Week 16
IRB-approved screening, consent, and collection protocols	Donor screening and eligibility determination	Blood draw and physical exam to confirm eligibility for donation	3-5 hour collection process depending on collection volume	First RUO LeukoPAC™ collection	First GMP LeukoPAC™ collection

100% Donor Recall Rate*

* Data reported for this project at the time of report publication.

LEUKOPAK COLLECTION

Using a ranked critical donor list, the client and OrganaBio were able to quickly move towards the next phase of the project – fresh RUO leukopak collections and shipment to the client's cell manufacturing facility in Singapore. Collection and shipment of one fresh RUO leukopak, initially at 2-8°C in a validated NanoCool shipper, demonstrated feasibility of the shipping logistics and acceptable product viability upon receipt, paving the way for shipment of critical raw materials for engineering runs and GMP manufacturing across the globe from Miami to Singapore. In addition to validating shipping methodology for each of the fresh RUO and GMP leukopak collections, OrganaBio scheduled the client's preferred donor as well as a backup donor to ensure material procurement at highly critical timepoints. Given the logistics of shipment to Singapore and CDMO manufacturing time slots, there was little room for a collection to be missed or delayed due to a donor issue.

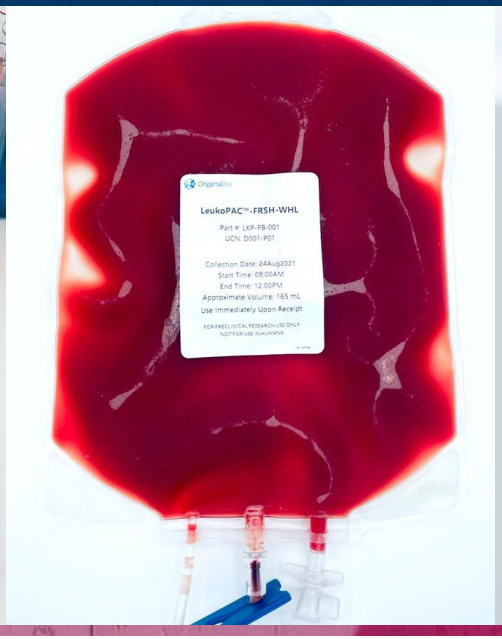
Although the first GMP leukopak collection needed to occur on a federal holiday to meet client and CDMO timelines, OrganaBio successfully scheduled a recallable donor for collection, completed the procedure, and delivered the fresh GMP leukopak on time to the client's CDMO in Singapore. Given OrganaBio's proximity to two international airports, OrganaBio has now successfully delivered several RUO and GMP leukopaks to Singapore to meet the client's rigid CDMO timelines.

Fresh LeukoPACs were shipped at 2-8°C in a validated NanoCool shipper

CONCLUSIONS & ACHIEVEMENTS

The client and OrganaBio worked towards a mutual goal of fresh GMP leukopak shipments to a Singapore CDMO facility to support manufacturing of IND-enabling studies. Our team facilitated a cost-effective plan for donor screening and curation of a reliable, recallable donor pool according to the client's specifications. This resulted in more than double the number of suitable donors for leukopak collections than the client had experienced in the past. Additionally, because OrganaBio manages the entire donor relationship process, the client was guaranteed an easy transition from RUO to GMP leukopak products using the same unique donor pool, saving them time and money in screening new donors for GMP use. Both teams worked together and successfully met tight CDMO manufacturing timelines, with OrganaBio delivering high quality fresh GMP leukopaks across the world.

Due to the success of the project, the client has extended the scope to screen more donors and is now beginning to procure GMP LeukoPACs for manufacturing of their NK cell therapy product.



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OrganaBio cGMP Manufacturing Facility
2420 NW 116th St, Suite 300
Miami, FL 33167

Ask about our new laboratory facility in Irvine, CA.

The new facility offers support services to clinical trial sponsors and CROs, including patient sample processing, analytical testing, cryopreservation, and storage.

Contact Us

References

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