PROJECT CASE STUDY:

TUMOR CELL ISOLATIONS

Development of a 100 Patient, Multi-Indication Tumor Cell Isolation Cohort for a Biomarker Discovery Study

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BACKGROUND:

The client in this case study is a Senior Director leading bioinformatics research and development for a healthcare company whose goal is to improve cancer treatment through diagnostic tools that enable early detection. The primary focus of their research is biomarker discovery for development of liquid biopsy tests in solid tumor indications. Discovery Life Sciences (Discovery) is proud to be a strategic partner to this innovative company since 2016, providing blood, plasma, and dissociated tumor cells (DTCs) samples from various solid tumor indications. This case study chronicles Discovery's timely provision of tumor cell suspensions from DTCs for this client's downstream sequencing applications.

Discovery recognizes the sensitive nature of our client's innovative research and therefore carefully and intentionally protects our client's identity throughout this case study.

REQUEST:

The study was ultimately segmented into 3 phases:

PILOT STUDY:

Processing of 10 high quality tumor cell suspensions from 4 fully consented patients in Discovery's biospecimen bank with 4 different oncology indications. The purpose of the pilot study was to establish baselines by indication for cell counts required to yield adequate DNA for sequencing.

PHASE 1:

Processing of 96 high quality tumor cell suspensions from 60 fully consented patients in Discovery's comprehensive biospecimen bank. Time was crucial for our client during this phase. Discovery met their strict timeline of 2 months for completion of this phase.

PHASE 2:

Prospective collection and processing of 85 high quality tumor cell suspensions from 36 fully consented patients with specific inclusion exclusion criteria.

THE AGGREGATED PARAMETERS FOR ALL PHASES OF THIS STUDY INCLUDED:

- 100 patients covering 9 solid tumor indications (191 total samples were processed due to the variability of tumor cell percentages within the indications)
- DTC samples must be characterized by flow cytometry for tumor and immune cell populations, as samples were selected based on tumor cell percentages
- Patients must be early stage and untreated
- Negative selection must be used to isolate the tumor cells
- Cell yields of >1 million were initially required, but this amount was reduced to 200k - 500k due to the excellent DNA yields demonstrated in the pilot
- The remaining positively selected cells from DTCs must be aliquoted and delivered to the client
- 1 additional DTC vial from each patient must be reserved until completion of the screening study

CONSULTATION:

Preparation of the dissociated tumor cell suspension for magnetic separation.

This project required initial consultations to determine the number of cells needed per patient sample, total number of DTC vials per indication, and timelines, as well as the development of a Material Transfer Agreement (MTA). Discovery's scientific and business development teams held multiple calls with the client to determine a detailed workflow for the project. It was decided that a pilot study would be beneficial in evaluating both expected cell counts from indications known to have lower tumor cell percentages and the number of cells required to get necessary DNA yields. During the pilot, the client confirmed the quality of the samples and the DNA yields for their downstream sequencing assays. The excellent DNA yields led to a reduction in the minimum cell count requirements from 1 million to 200k - 500k tumor cells per patient sample. Additionally, the baseline cell count data by indication lead to optimized selection criteria for evaluating the DTC flow characterization reports. Discovery then provided accurate quotes and timelines for the completion of the remainder of the project.

During phase 1 of the project, the client had firm deadlines and our team consulted with them to determine an isolation schedule of 10-15 patients per week to complete the 60 patients (96 samples) requested within 2 months. During the first month of phase 1, other scientific consultations occurred to further optimize the sample selections and yields per indication.

TUMOR CELL ISOLATION PURITY, VIABILITY, AND YIELD BY INDICATION

	Pre Selection EpCAM+ %	Post Selection EpCAM+ %	Post Selection Viability	Yield
Indication	**Average**			
Bladder	59.70%	96.40%	80.10%	62.70%
Breast	65.20%	93.90%	86.00%	65.70%
Colorectal	53.30%	94.90%	86.00%	35.70%
Endometrial	55.50%	95.00%	81.00%	38%
Gastric	36.30%	92.60%	86.70%	46.90%
Kidney	27.40%	89.20%	76.70%	52.80%
Lung	22.80%	96.20%	83.60%	59.90%
Ovarian	58.10%	96.30%	82.60%	41.70%
Pancreatic	47.30%	96.30%	94.60%	100%
Total	49.20%	94.60%	83.60%	50.50%

For each indication, the percentage of EpCAM+ tumor cells was determined both pre- and post-selection by flow cytometry. Yields were determined by comparing the number of tumor cells expected, based on pre-selection EpCAM+ percentages, versus the number of tumor cells following post-selection. These data are representative of the average isolation expected for each indication.

FULFILLMENT:

After the initial pilot study was completed and the phase 1 timeline was established for processing samples from Discovery's comprehensive biospecimen bank, our laboratory completed and delivered samples from all 60 patients (96 samples) within the two month timeline. Then in phase 2, all incoming tumor samples matching the remaining study criteria (indication, disease stage, cell population percentages, etc.) were processed and delivered within 6 months, which met all the client's expectations.

The bioinformatics group confirmed their satisfaction with the quality of the samples Discovery produced, aligning with the expectations drawn from previous studies conducted with us. All sample deliveries were coordinated with the client by the project's dedicated project manager at Discovery, so no shipping delays or logistical issues occurred.

SUCCESS:

The bioinformatics director was very pleased with the outcome of this project. They were able to meet their goals and deadlines for the early phases of their liquid biopsy biomarker discovery project. Plans for future projects including patient matched DTCs with blood samples and NGS services conducted in Discovery's laboratories are currently being discussed.

This study was successful because the client was:

- Able to access a large volume of characterized DTCs across many solid tumor indications.
- Provided custom consultations to develop the parameters and workflow that would meet their specific research needs.
- Assured that the tumor cell isolations resulted in high quality DNA yields.
- Provided quick and clear communication throughout the project, from the initial consult through to fulfillment.
- Able to complete their research goals on time and on budget

NEW SERVICES AVAILABLE NOW:

Since the initiation of this project, Discovery has developed additional high quality scientific laboratory services to accelerate similar projects. These services include:

- HudsonAlpha Discovery NGS profiling of cell populations within DTCs
- Cell culturing services such as exansion, activation, tumoroid development, etc.
- Flow cytometry services such as marker discovery, receptor expression, etc.

Accelerate your study by contacting Discovery at info@dls.com or learn more about our comprehensive biospecimen and laboratory services at www.dls.com