SLINGSHOT

CASE STUDY

The Slingshot Difference:
Development of a Ki-67 expressing cell mimic for assay validation at Cerba Research

CLIENT
Cerba Research

THERAPEUTIC AREA
Immuno-oncology

PROJECT OVERVIEW

Cerba Research is a clinical trial service provider offering central and specialty laboratory solutions as well as medical device and IVD services in a wide range of therapeutic areas including oncology. To better support their client services, the Cerba Research Flow Cytometry team collaborated with Slingshot Biosciences to develop a lymphocyte cell mimic embedded with Ki-67 to be used in the validation of one of their assays.

Ki-67 expression in immune cells is dependent upon cellular activation and rarely expressed in cells at steady state. Due to the low frequency of Ki-67 expressing cells, Ki67 is defined as a "rare marker" when it comes to validation of Flow Cytometry assays. To validate such rare markers, activated cells or surrogate cells (such as lyophilized cells or a cell line) are spiked into the matrix of interest. However, activation of cells from the same donor prior to assay validation experiments creates logistical difficulty and might add unforeseen variability in the data. Ki-67 expressing control materials are not commercially available. This situation impacted Cerba Research's ability to validate an assay with Ki-67-related endpoints in a clinical trial. For this reason, Cerba Research contacted Slingshot Biosciences to develop a Ki-67 control that would allow the team to validate Ki-67-related endpoints according to CLSI H62 guidelines.

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CUSTOMER CHALLENGES

During validation of a flow cytometry assay which is designed to detect changes in Ki-67 as an indication of drug effect, the Cerba Research Flow Cytometry team realized that there were no readily available Ki-67 cellular controls that would allow them to validate Ki-67-related endpoints in their biological samples.

OUTCOMES

This is where Slingshot Biosciences was able to provide a solution. Dr. Veronica Nash, US Regional Head of Flow cytometry at Cerba Research, states “Slingshot Biosciences demonstrates its adaptability to generate controls that truly mimic biological expression”.

This control has since enabled Cerba Research to proceed with their project in a timely manner and meet the drug evaluation and testing needs of their customers. Dr. Nash describes it as “a game changer for our project.” She also states that “the collaboration between Cerba Research and Slingshot Biosciences on this project will have an important impact for Flow Cytometry controls not yet available on the market. The power of Slingshot’s technology is so far unchallenged and requires researchers to reach out and ask for the biomarker controls that they need.These cell mimics have the potential to fill gaps in the lack of rare marker controls needed for assay validation”, Dr. Nash concludes.

Slingshot Biosciences now has Ki-67 controls available for purchase through Slingshot Labs.

Visit us at slingshotbio.com to learn more.

SOLUTION

Slingshot Biosciences leverages biochemistry, high-precision manufacturing, and polymer chemistry to engineer cell mimics with tunable size, morphology, and biochemical properties that can be matched to any cell type. Using this technology, the Slingshot team produced a lymphocyte mimic expressing Ki-67 at Cerba’s desired MFI.
After Slingshot determined the appropriate attachment chemistry for the lymphocyte mimic, they provided Cerba Research with several candidates to test.

Figure 1, on following page, shows data provided by Cerba Research to the Slingshot team demonstrating the desired expression pattern of the Ki-67 cell mimic to resemble biologically relevant samples.

As requested, Slingshot was able to mimic a spread in MFI expression with clear separation from the negative population. Furthermore, Slingshot provided data for Ki-67 cell mimics designed to bind Cerba Research’s antibody as a clear positive/negative control.

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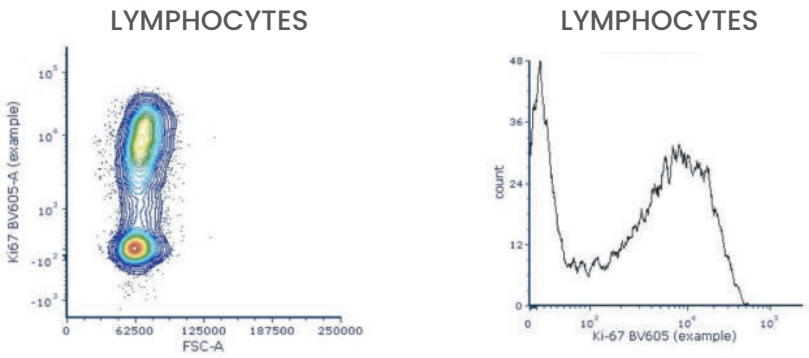

FIGURE 1: Cerba Research provided dot plot and histogram of desired Ki-67 expression.

Figure 1 shows data provided by Cerba Research to the Slingshot team demonstrating the desired expression pattern of the Ki-67 cell mimic to resemble biologically relevant samples

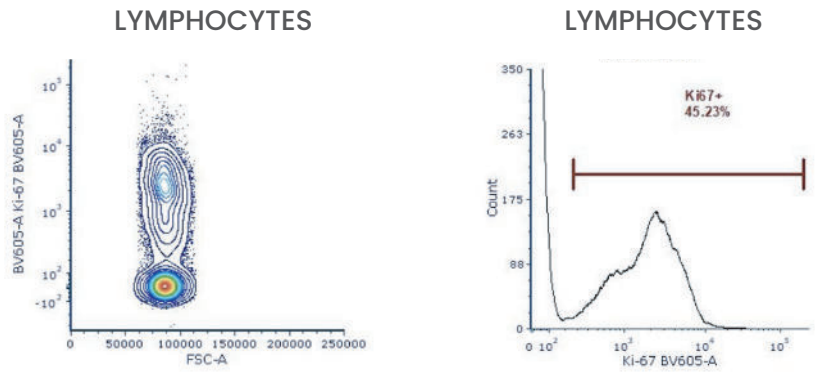

FIGURE 2: Dot plot and histogram of Cerba Research's validation of Slingshot provided Ki-67cell mimic

The Cerba Research team tested the provided product in their assay. Results showed that the cell mimic product, after spiking in biological samples, could be specifically detected by anti-Ki-67 antibody used in the assay and suitable for validation experiments (Fig 2).

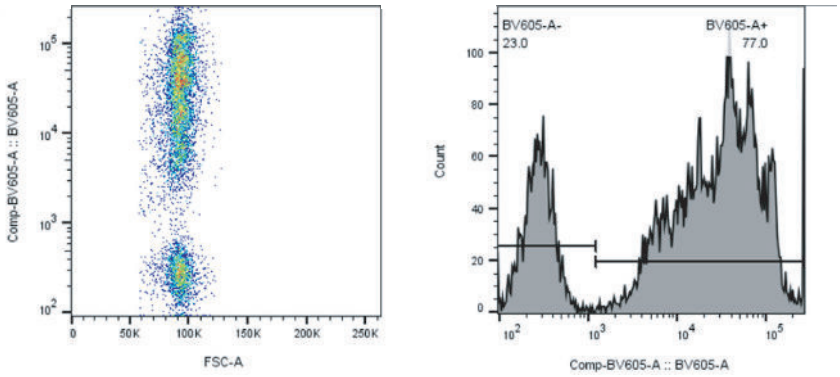

FIGURE 3: Dot plot and histogram of improved MFI expression Ki-67 cell mimic stained with BV605 anti-Ki-67 antibody clone Ki-67

After confirming the antibody binding and detection, Slingshot provided an improved final product that reproduced the natural spread of Ki67 and increased the maximum MFI of the Ki-67 population to more accurately recapitulate the Ki-67 "smear" seen in cells (Fig. 3).