Deployment of a visualization tool directly linked to CellEngine cytometry analysis software to accelerate analysis of complex cytometry data sets in the context of ongoing clinical trials

Damien Montamat-Sicotte[1], Zach Bjornson[1], Dean Franckaert[1], Eustache Paramithiotis[1], Nick Dupuis[1]
CellCarta[1], 201 Av. du Président-Kennedy Suite 3900, Montreal, Quebec H2X 3Y7

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CellCarta

SUMMARY

High-dimension cytometry panels have become a hallmark of clinical phase 1 and 2 trials. These panels can provide hundreds of readouts and need to be combined with subject metadata (e.g., health data, demographics, timepoint, and dose) to provide insights on biomarkers. Several bioinformatics tools are available to interpret these complex datasets; however, these usually require significant expertise in data manipulation, which sometimes forces the person doing the data interpretation to outsource the data visualization and statistical analysis to a bioinformatics team. As a consequence, the scientist can be one step-removed from the "raw" data, critically preventing the interpretation of biomarker effects in the context of the raw staining profiles and associated quality controls (e.g. in-run controls). Here, we show how a new tool integrated within the CellEngine cytometry analysis software that can accelerate data interpretation without removing the scientist from the raw data.

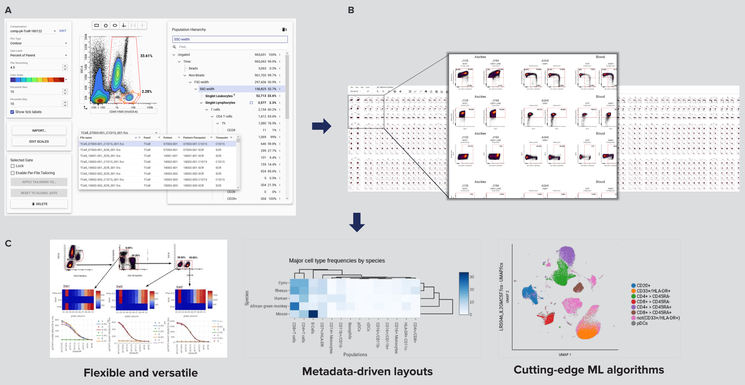

Figure 1. CellEngine is a cloud-based cytometry analysis software that is designed to analyze large data sets with a metadata-guided workflow and a global-first analysis for high level of rigor. A) Visual example of gating interface. B) CellEngine allows visualization of large data sets within its layout feature, allowing to easily and quickly verify large data sets and change the gating individually or in a group-manner. C) CellEngine offers a variety of visualization tools in addition to clustering algorithms.

METHODS

The visualization tool pulls live data from CellEngine, displaying both study- and cohort-level information in summary views as well as the sample-level staining profiles. As a live link, any changes made in CellEngine, such as ones to gating and compensation, or the addition of new samples during an ongoing study, are automatically reflected in the dashboard. This link also gives the ability to consult staining profiles and performance of controls directly within the tool without having to switch between applications. CellEngine is capable of analyzing 10,000s of samples at once, and thus can handle the largest of studies.

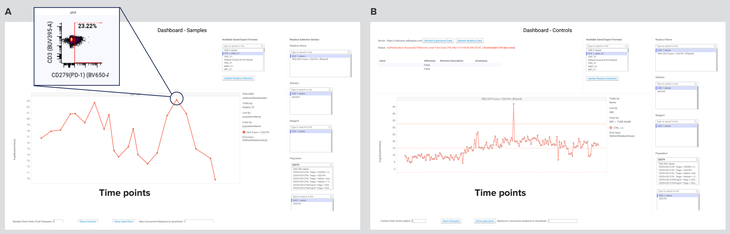

Figure 2. Example of visualization tool (Dashboard) interface. A) PD-1 expression shown in a subject across multiple timepoints with the ability to consult the PD-L1 dot plot with gating for each time point. B) Trending of the CD-Chex control associated with each run across the full length of the program, allowing easy appraisal of the performance of the different runs.

RESULTS

In this first example, we show how the visualization tool was used to monitor the effect of treatment using a TBNK assay in 7 subjects. B cell population was tracked longitudinally across multiple timepoints. The visualization tool was used to look at the performance of the two inter-run controls to easily identify which timepoints should not be considered during analysis. In addition, with the direct link to CellEngine, dot plots were monitored within the interface of the visualization tool to assess quality of staining profiles, allowing quick and in-depth interpretation of the flow cytometry data.

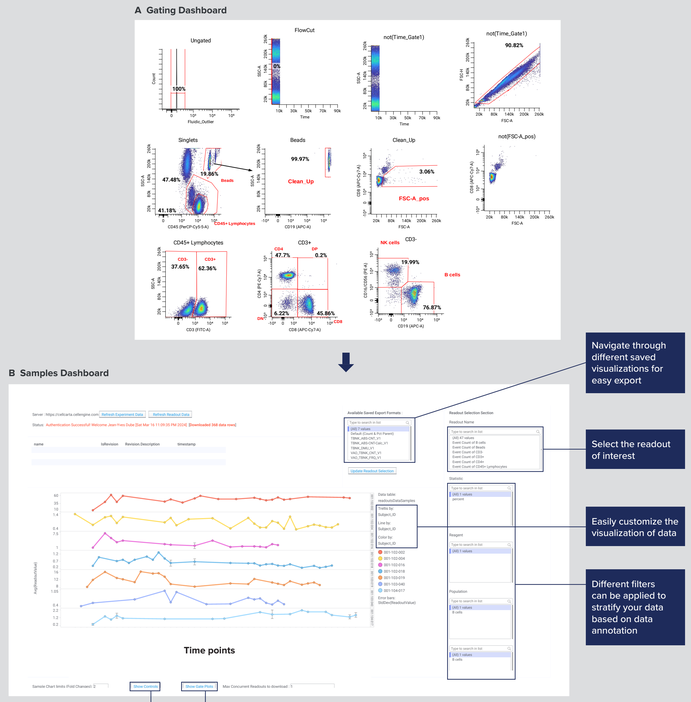

Figure 3. Results from a TBNK assay deployed in 7 subjects were plotted using the visualization tool to track the effect of treatment on B cells. A) Gating hierarchy performed in CellEngine. B) B cell absolute counts were tracked longitudinally across multiple timepoints using the visualization tool. C) Using the tool's "Show Controls" feature, the performance of the two inter-run controls was monitored across all runs. D) Using the tool's "Show Gate Plots" feature, the staining profiles of a particular timepoint were consulted for the subject's sample and the two inter-run controls.

In this second example, we show how the visualization tool was used to monitor CD4+ T cell IFNγ responses from an intra-cellular cytokines staining assay (ICS) following stimulation in three subjects across multiple timepoints. After careful gating within CellEngine, the IFNγ responses from 3 subjects were plotted on the same graph to understand variability of the responses across different timepoints following treatment. In addition, the staining profile for responses against SEB was consulted for a particular subject sample.

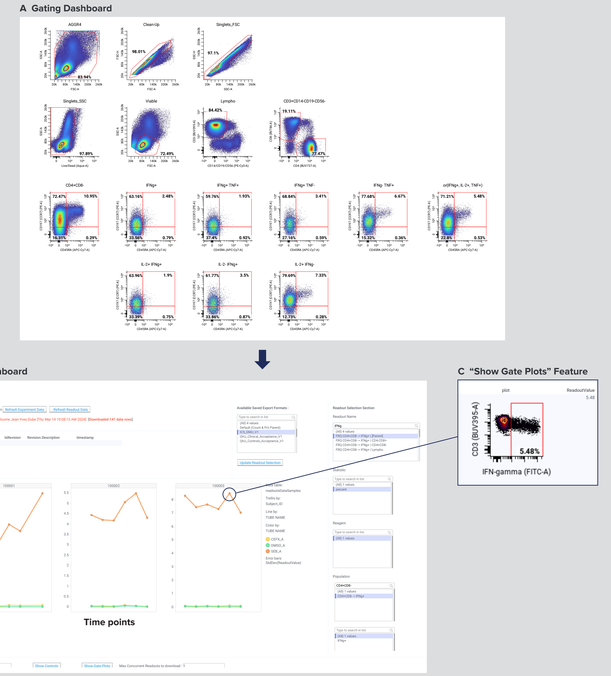

Figure 4. Results from an ICS assay deployed in 3 subjects were plotted using the visualization tool to track the effect of treatment. A) Gating hierarchy performed in CellEngine. B) CD4+ T cell IFNγ responses were tracked longitudinally across multiple timepoints in 3 subjects. C) Using the tool's "Show Gate Plots" feature, the staining profile of a particular timepoint was consulted for the SEB stimulation condition.

CONCLUSIONS

This new tool can help maximize the utility of high-dimensional cytometry in clinical trial analysis while allowing to keep the crucial link between graphical representation of large number of samples and the data associated with each individual flow cytometry staining profile. The next evolution of this tool will allow the monitoring of results from different platforms to approach data in a true multi-omics fashion, this way of visualizing the data would allow maximization of the understanding of different data sets.

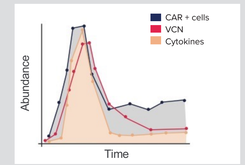

Figure 5. Example of visualization of data-sets from flow cytometry, PCR and MSD shown in one graph – upcoming feature in CellEngine.

Please send inquiries to
Damien Montamat-Sicotte
Scientific Business Director
damien.sicotte@cellcarta.com