High dimensional biology with high throughput multiomic profiling of single cells

Aruna Ayer[1], Hye-Won Song[2], Larry Wang[1], Devon Jensen[1], Chelsea Gordon[1], Yan Chen[1], **Jamie Moskwa**[1], **Jody Martin**[1], **Tracy Campbell**[1], **Adam Wright**[2], **Zhiyuan Han**[1], **Gracia Genero**[1], **Raghavendra Padmanaban**[1], Hongduan Huang[1], Quyen Bao[1], Ruifang Li[1], Thomas McCarthy[1], Rosary Nguyen[1], Ricelle Acob[1], Cynthia Sakofsky[1], Manish Takran[1], Samatha Vadreru[1], Joe Olives[2], **Elham Hatami**[2], **Zhiqi Zhang**[2], **Samuel Shi**[1], **Punya Narayan**[1], **Lin Chen**[1], **Anne Tran**[1], **Yingwah Lee**[1], **Amie Radenbaugh**[1] Youngsook Kim[1]

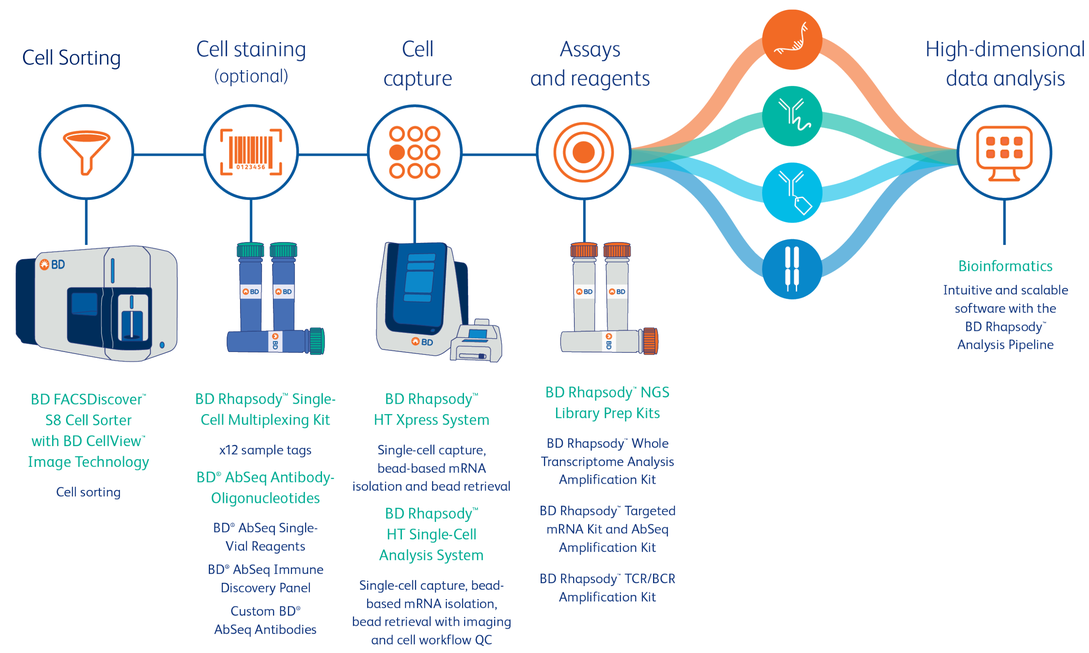
[1]*BD Biosciences 2350 Qume Drive, San Jose CA;* [2]BD Biosciences 10975 Torreyana Rd, San Diego CA

Abstract

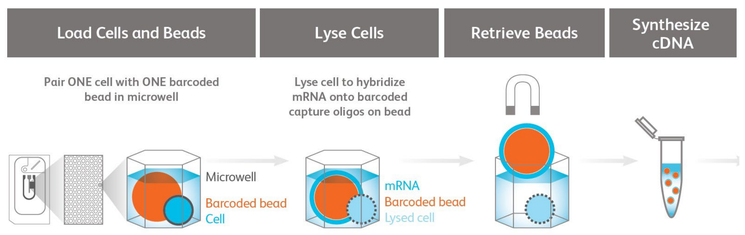
Flow cytometry technology remains one of the most powerful tools used by life scientists to analyze single cells and characterize the cell at the protein layer. As biologists have sought to know more, the single “ome” of proteins alone could not fully explain cellular complexity. Single cell multiomics provides a comprehensive view of the cellular heterogeneity and the complex interplay between multiple layers of cellular "omics", namely the DNA, RNA and protein layers. Researchers are increasingly applying single cell multiomics across many fields including cancer research, drug discovery, infectious disease research and more.

Here in, we present data to showcase how BD Rhapsody HT-Xpress System fits within a reliable end-to-end single-cell multiomic solution with upstream cell-sorting solutions and downstream single-cell multiomic assay kits and bioinformatic tools. The gentle and robust micro-well based high throughput single-cell partitioning system featuring a flexible 8-lane cartridge design that can process up to half a millions cells per cartridge. Cell capture rates are typically > 80%, even with cells of varying sizes and fragility, including neutrophils and natural killer cells and even nuclei. The comprehensive single-cell multiomic assays include DNA chromatin accessibility assay (ATAC-seq), targeted/whole transcriptome assay (WTA), TCR/BCR full-length sequencing assay and CITE-seq assay with Abseq antibody oligos for surface and intracellular protein profiling. We present data highlighting the sensitivity and specificity of these multiomic assays and showcase the depth of molecular information and discovery enabled by single-cell multiomics.

End to end single-cell multiomic workflow



BD Rhapsody™ - Flexible, high-throughput platform for single-cell multiomics

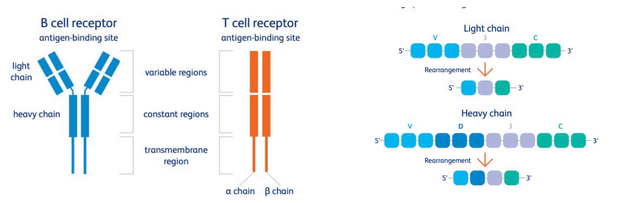


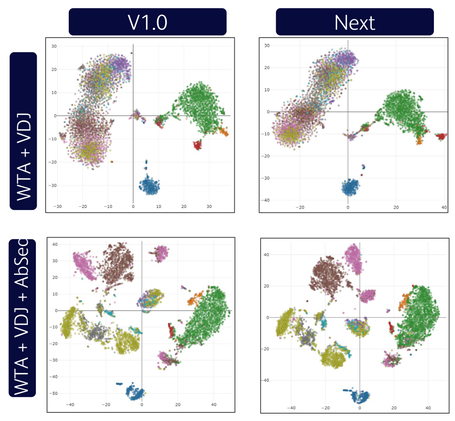
- Flexible, higher throughput cell capture with gentle micro-well technology
  - -Load up to 500,000 cells per 8-lane cartridge, 100-65K cells per lane.
  - -Partial use cartridge stable up to 6 months
  - -cDNA on beads stable up to 1 year.
- Whole/Targeted transcriptome (mRNA), CITE-seq (mRNA+surface/intracellular protein), TCR/BCR Multiomic Assay (VDJ+mRNA+surface protein) assays, ATACseq (Standalone or multiomic chromatin DNA/mRNA Assay)
- No batch effect between lanes and cartridges.
- No sample loss due to clogging

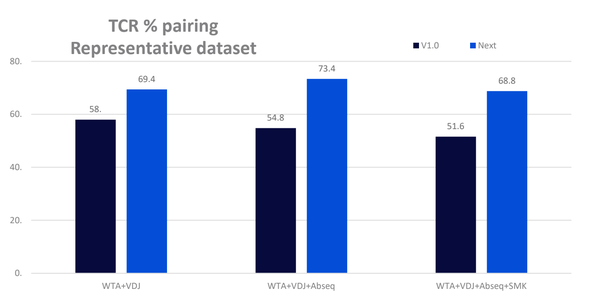
BD Rhapsody™ TCR/BCR Next Multiomic Assay

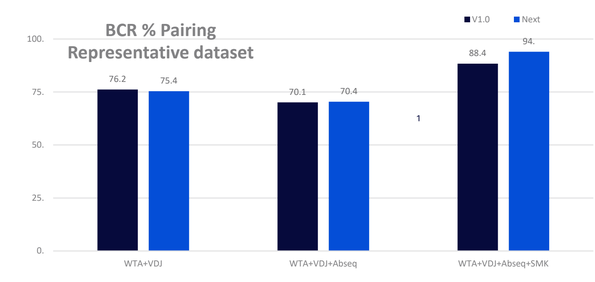
Multiomic TCR/BCR sequencing assay with whole transcriptome and surface protein profiling

<u>Next</u> assay launching soon with improved full-length TCR pairing efficiency compared to V1.0 assay



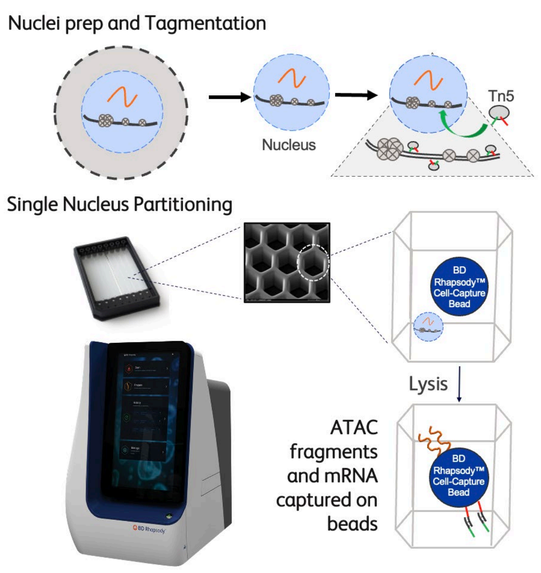


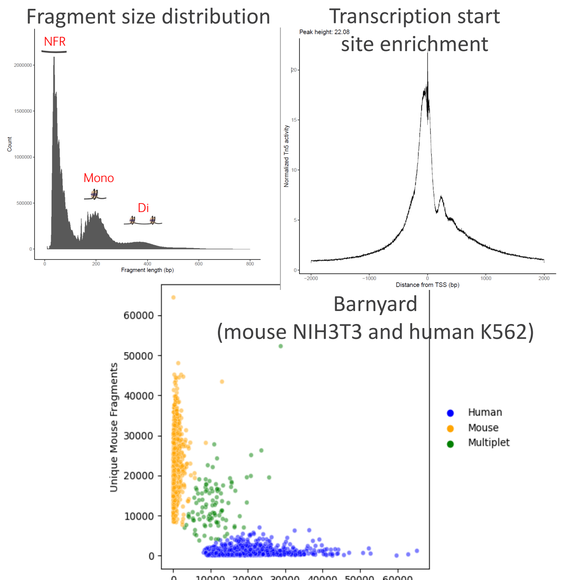




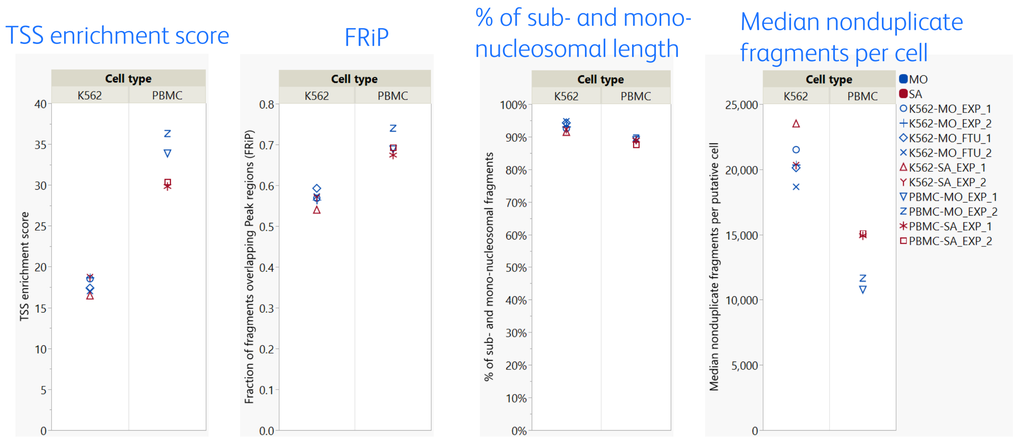
BD Rhapsody™ ATAC-Seq Assay

Standalone or multiomic single-nuclear chromatin accessibility assay with whole transcriptome



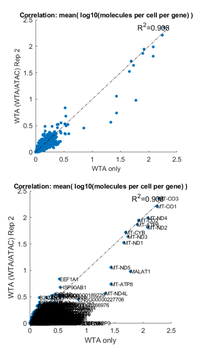


High specificity and sensitivity assay to profile open chromatin regions of the genome



Sequencing depth: ~50,000 raw read pairs per putative cell

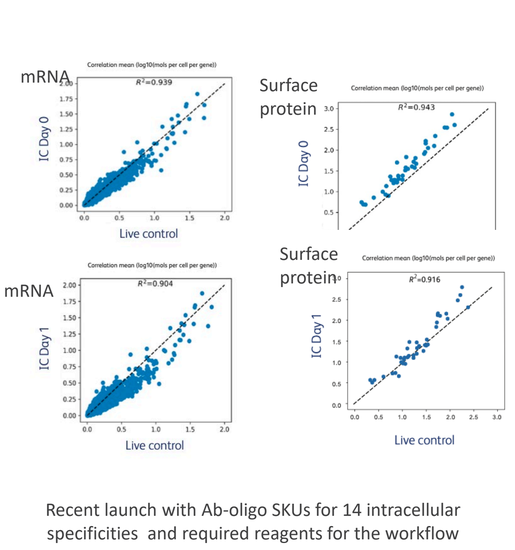
Gene expression correlation between WTA +/- ATAC



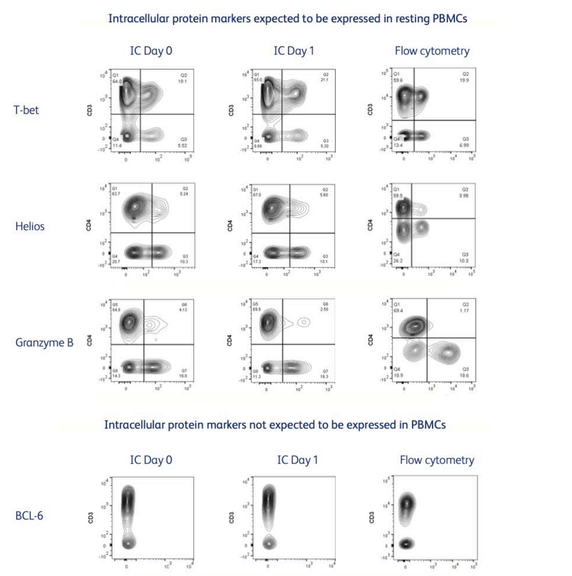
Representative dataset

BD Rhapsody ™ Intracellular CITE-seq Assay

Simultaneous profiling of <u>RNA with surface and intracellular proteins</u> on the BD Rhapsody™ System



Recent launch with Ab-oligo SKUs for 14 intracellular specificities and required reagents for the workflow



BD OMICS-Guard™ Sample Preservation buffer

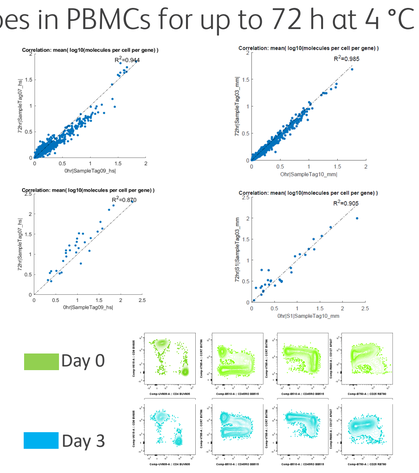
PFA-free buffer that preserves RNA and protein epitopes in PBMCs for up to 72 h at 4 °C

Biological sample preservation is a critical need

- De-centralized sample collection
- Longer sample processing times
- Large-scale population studies

Available in two formats:

- 50-mL bottle
- 12 x 1-mL vials



Conclusions

In summary, we show case how high parameter spectral flow cytometry with real-time imaging and flexible/high-throughput single-cell multiomic assays to profile DNA/RNA/protein enable deeper biological insights.