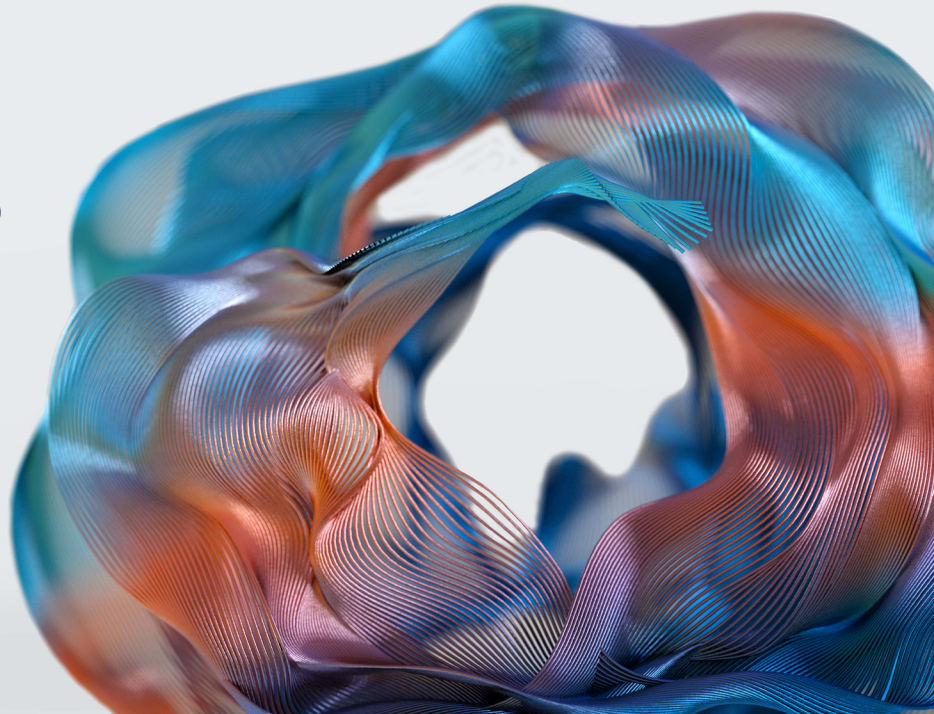


ResolveOME

Whole Genome and
Transcriptome Amplification System:

Enabling Comprehensive Single-Cell Multiomic Analysis



BioSkryb's ResolveOME™ Whole Genome and Transcriptome Amplification System combines our breakthrough whole-genome amplification (WGA) technology, Primary Template-directed Amplification (PTA), with full-transcript reverse transcription and our innovative BaseJumper™ computational tools to pave the way for comprehensive single-cell multiomic analysis. Capable of near-complete coverage of the genome and mRNA transcriptome, the ResolveOME System melds genome variation data with transcriptional and translational layers of information to provide a more complete picture of the drivers and consequences of clonal heterogeneity and enables insights into the identity, role, and fate of individual cells.

ResolveOME Key Highlights:

- **Complete genome and full-length mRNA coverage** reveals the consequence of genomic variation (all major variant classes) on gene expression and transcript structure, and exposes subtle changes in protein sequence that may profoundly impact structure, function, and activity.
- **A unified workflow** for the interrogation of DNA and RNA from the same cell obviates the need for splitting source material or interpret across data sets.
- **Full transcriptome workflow enables enhanced RNA analysis** compared to droplet-based single-cell RNA sequencing, providing full transcript RNA-Seq, splicing and isoform detection, and gene fusion detection.

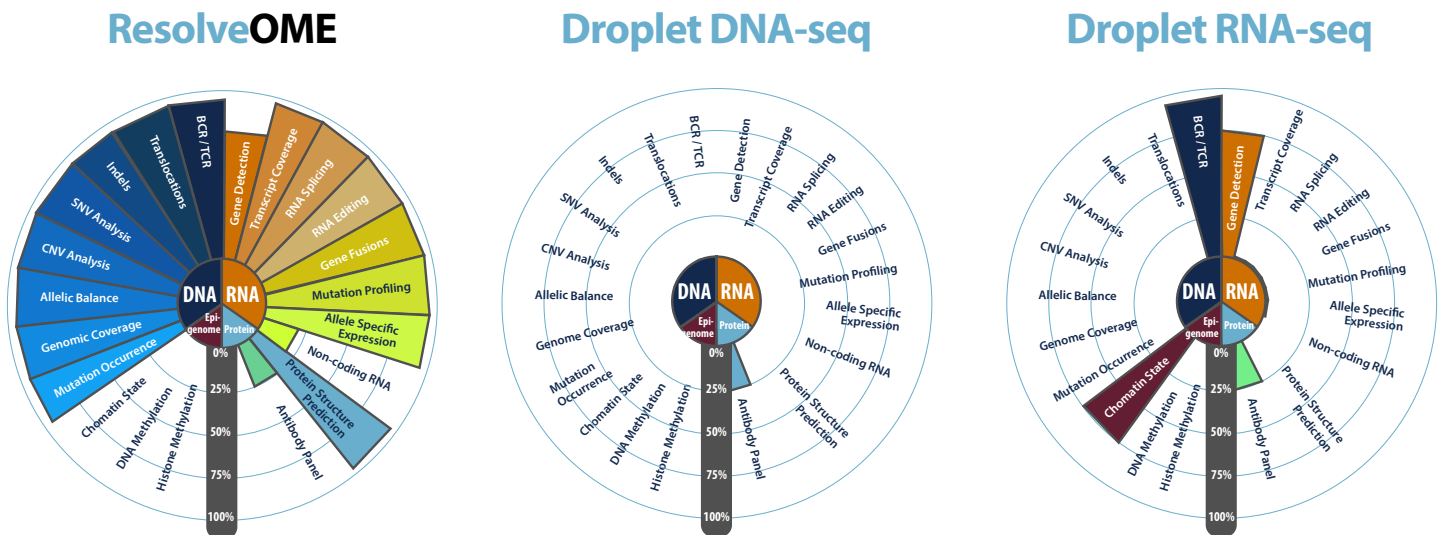
Breadth of Coverage

Comprehensive, high-quality data hold the key to actionable multiomic analysis

The cell is the fundamental unit of biology. Bulk (multicellular) analysis methods limit our ability to understand intricate molecular relationships, whereas existing single-cell methods offer limited coverage of the macromolecules that work in concert to determine cell development and disease states. In particular, the shortcomings of traditional WGA methods have hampered the integration of single-cell genomic data into multiomic data sets.

The ResolveOME Whole Genome and Transcriptome Amplification System utilizes BioSkryb's highly uniform and accurate PTA WGA technology¹ in a novel workflow that allows for the simultaneous, parallelized analysis of the entire genome and polyadenylated transcriptome of individual cells. Unlike droplet-based single-cell technologies, The ResolveOME Whole Genome and Transcriptome Amplification System yields integrated, high-quality data on all major classes of genetic variation (SNVs and indels, CNV, and structural variants) in both DNA and RNA. ResolveOME enables analysis of the co-occurrence of mutations, tumor mutation burden (TMB), and homologous recombination repair deficiency (HRD). Genome-based mutation profiling—used in combination with curated databases (ClinVar, COSMIC) and established algorithms—allows for the annotation of coding changes that impact the structure and function of every encoded protein and the risk-based prediction of concomitant changes in protein activity, with far greater depth and breadth than antibody-mediated detection methods.

Elucidate molecular mechanisms and biological pathways with confidence, to blaze a trail toward the discovery of actionable biomarkers and putative drug targets.



Breadth of data accessible with the ResolveOME Whole Genome and Transcriptome Amplification System. Unlike droplet-based single-cell DNAseq and 3'-end counting RNAseq platforms, the ResolveOME workflow offers a comprehensive view of the genome, mRNA transcriptome, and inferred impacts of protein sequence alterations. The ResolveOME Whole Genome and Transcriptome Amplification System supports more modalities (number of segments), and typically offer more complete coverage within individual modalities (length of segments, normalized to 100%). Although droplet-based methods offer one to two logs higher throughput, the ResolveOME System yields data from a significantly higher proportion (>3-fold) of input cells. Data dials were generated using a combination of quantitative and qualitative internal data and published data.

Unified Workflow

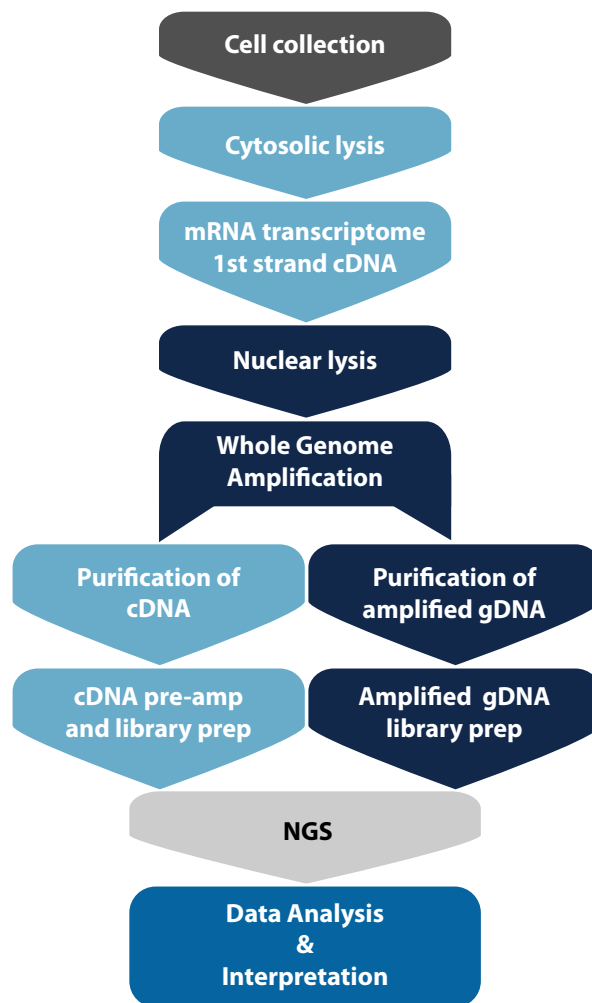
Unified workflow enables DNA and RNA analysis from the same cell

Existing methods for combined DNA and RNA sequencing typically rely on the construction of separate DNA and RNA (cDNA) libraries from a bulk sample, with data integration occurring post sequencing. This requires a significant amount of input material and cross-referencing of data, thereby increasing the risk of sample processing and computational error. In addition, such bulk sequencing approaches lack the resolution needed to fully understand the molecular and cellular dynamics of biological systems.

The ResolveOME Whole Genome and Transcriptome Amplification System utilizes a novel, unified workflow that allows for the construction of a whole genome and full-length mRNA library from the same single cell. Isolated cells undergo cytosolic lysis to permit reverse transcription (1st strand synthesis) of mRNA with a template-switching protocol. Nuclear membranes are subsequently disrupted to allow for even and accurate amplification of genomic DNA with BioSkrbyb's Primary Template-directed Amplification (PTA) technology. Only at this stage is amplified genomic DNA and cDNA separated for library construction using established methods. Barcoded libraries may be pooled for sequencing. Sequencing data is combined in the BaseJumper™ Bioinformatics Platform for analysis, visualization, and interpretation.

The unified ResolveOME workflow:

- **Only requires a single cell** for the construction of a whole-genome and full-length mRNA transcriptome library but is compatible with bulk sample inputs.
- **Is completed in 2 – 3 days**, from cell sorting to sequencing-ready libraries, with less than 9 hours of hands-on time.
- **Provides the same quality WGA performance as ResolveDNA:** PTA leads to reduced amplification artifacts, >97% genomic amplification coverage and improved allelic balance compared to traditional MDA.



Integrated ResolveOME workflow. Sequential disruption of cellular and nuclear membranes allow for first-strand cDNA synthesis and WGA to be performed in the same tube, without intermediate cleanup steps. Construction of RNA libraries include a pre-amplification step. Target enrichment of cDNA and/or whole-genome libraries may be performed if required.

Applications

The ResolveOME Whole Genome and Transcriptome Amplification System supports applications that require broad and deep characterization of genomic variation and full-length mRNA transcripts. Examples include:



Cancer Genomics

Find, characterize, and track the conserved, rare, and *de novo* variant alleles that drive outcomes.



Neurology

Detect rare somatic mutations in single neurons with high accuracy and precision.



Cardiology

Integrate single-cell genomics to obtain a complete picture of the genetic basis of CVDs.



Immunology

Comprehensively analyze individual cells in immune repertoires.



Preimplantation Genetic Testing

Base critical pre-implantation decisions on comprehensive embryo screening.



Microbiome Research

Obtain and characterize near-complete genomes from individual bacterial cells.



Toxicology

Interrogate mutations and off-target gene editing at single-cell resolution.



Bioprocessing

Detect trace amounts of biological contaminants with confidence.

References:

- 1 Gonzalez-Pena V, et al. *Proc. Natl. Acad. Sci. U.S.A.* 2021; 118 (24): e2024176118; doi: [10.1073/pnas.2024176118](https://doi.org/10.1073/pnas.2024176118)

At BioSkryb Genomics, we are ushering in a new era of single-cell multiomics. Our technology provides unparalleled genomic and transcriptomic resolution in single cells. See what you have been missing!

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