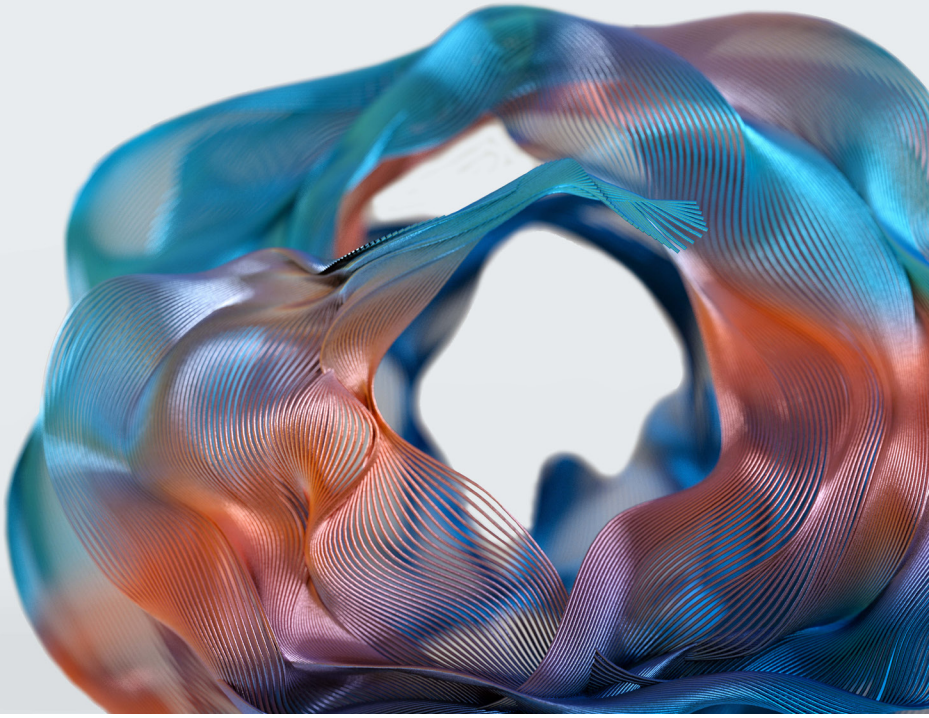
BioSkryb GENOMICS

Cells explored. **Answers revealed.**

ResolveOME

Whole Genome and Transcriptome Amplification Kits:

Enabling Comprehensive Single-Cell Multiomic Analysis



BioSkryb's ResolveOME Whole Genome and Transcriptome Amplification Kits combine 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, ResolveOME Kits meld genome variation data with transcriptional and translational layers of information to provide a more complete picture of the drivers and consequences of clonal heterogeneity within cell populations than ever before.

The ResolveOME unified single-cell workflow enables insights into the identity, role, and fate of individual cells that are:

- **Comprehensive:** >90% 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.
- **Accurate:** 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.
- **Versatile:** compatible with all viable, fresh/frozen cells to support a wide range of applications in oncology, neurology, immunology, cardiology, reproductive medicine, microbiology, toxicology, and bioprocessing.

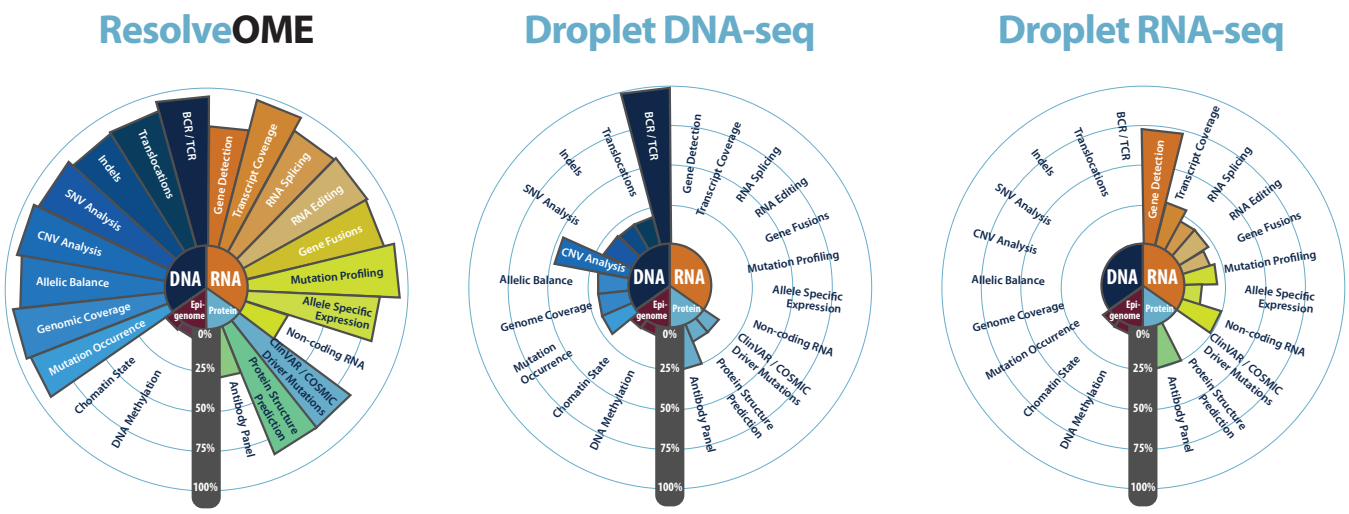
Breadth of Coverage

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 Kit utilizes BioSkryb's highly uniform and accurate PTA WGA technology[1] 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, ResolveOME Whole Genome and Transcriptome Amplification Kits yield 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 Kit. 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. ResolveOME Whole Genome and Transcriptome Amplification Kits support 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, ResolveOME Kits yield data from a significantly higher proportion (>3-fold) of input cells. Data dials were generated using a combination of quantitative and qualitative internal and published data.

Unified Workflow

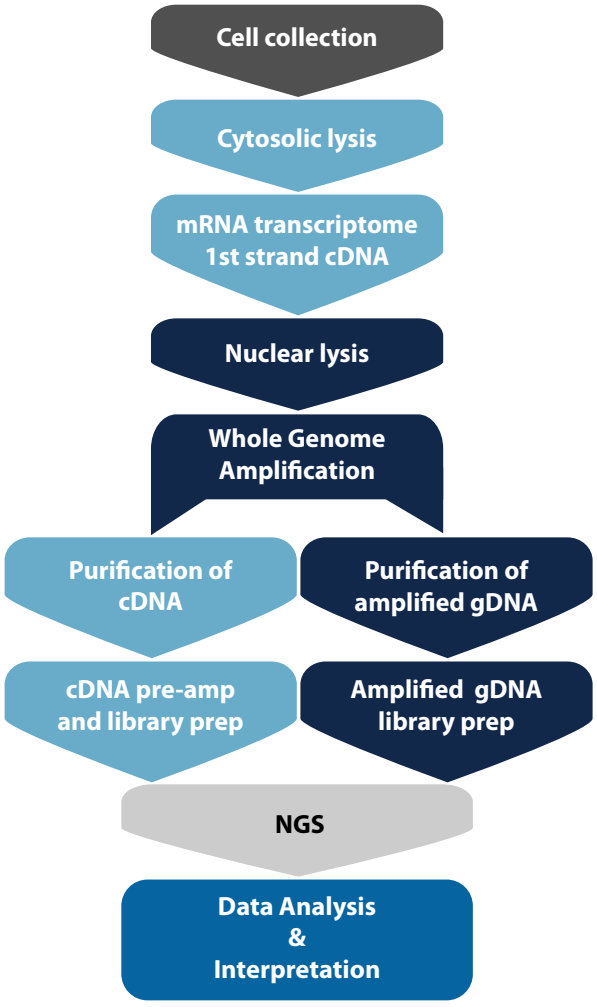
Unified workflow enables DNA and RNA analysis from the same cell

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 Kit 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 BioSkryb'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.
- Is ideally suited for projects involving **fewer cells due to the depth and quality of generated data.** High-quality data is typically obtained from >90% of samples.



Integrated ResolveOME workflow. Sequential disruption of cellular and nuclear membranes allow for first-strand cDNA synthesis and WGA to be performed in the 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

ResolveOME Whole Genome and Transcriptome Amplification Kits support 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.

Contact us today to be the first to experience a new era of multiomic analysis

Apply to be part of our ResolveOME Early Access Program (EAP) and receive the following benefits:

- Access to a complete ResolveOME Kit
- In-person training at our headquarters in Durham, NC
- Sequencing services (available upon request)
- Pre-launch access to BaseJumper™ bioinformatics platform
- Collaborate with our scientists to advance your work

Apply Today!

References:

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

BioSkryb GENOMICS

info@bioskryb.com
www.bioskryb.com

Phone: 1-919-370-0841
Twitter: @BioSkryb

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