# A revolution in resolution

Introducing

## ResolveOME

Enabling Comprehensive
Single-Cell Multiomic Analysis

BioSkryb GENOMICS

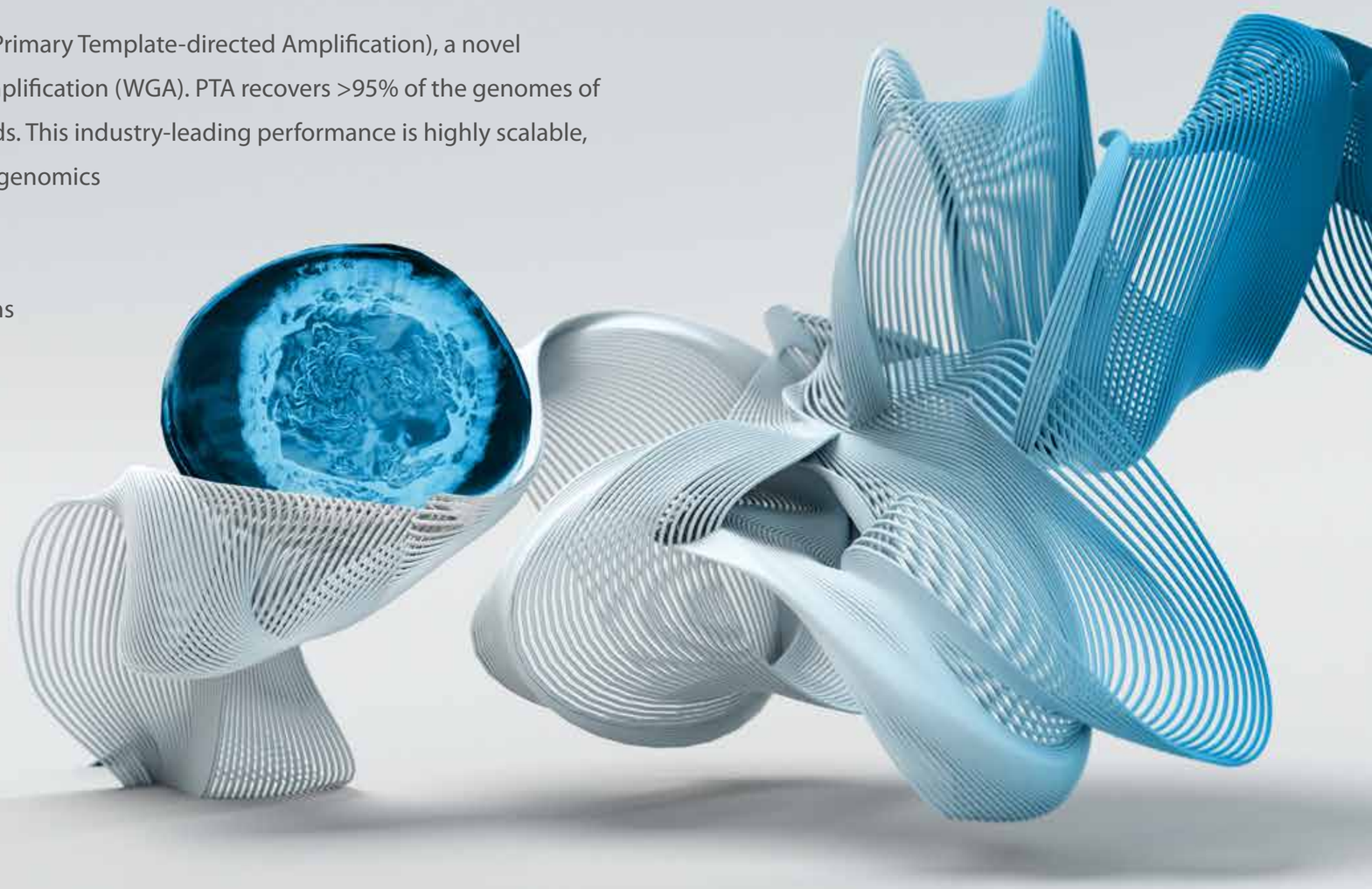
Cells explored. Answers revealed.

# Powering a genomics revolution with superior resolution

**Massively parallel bulk sequencing has vastly expanded our knowledge of the living world. However, higher resolution is needed to understand and leverage the contributions of individual cells to the biology of organisms and ecosystems.**

BioSkryb is revolutionizing the field of single-cell genomics with PTA (Primary Template-directed Amplification), a novel technology that enables accurate and reproducible whole genome amplification (WGA). PTA recovers >95% of the genomes of single cells with higher fidelity and uniformity than other WGA methods. This industry-leading performance is highly scalable, supporting robust, reliable and routine single-cell and ultra-low input genomics applications in clinical, translational and life sciences research.

BioSkryb is developing complete sample-to-analysis workflow solutions for variant detection and characterization from single-cell and ultra-low input samples. Our PTA-based ResolveDNA™ Whole Genome Amplification Kits form the core of whole genome and targeted sequencing workflows, enabling single-nucleotide variant (SNV) and copy number variant (CNV) analysis in cancer genomics, cardiology, neurology, immunology, toxicology and preimplantation genetic testing.

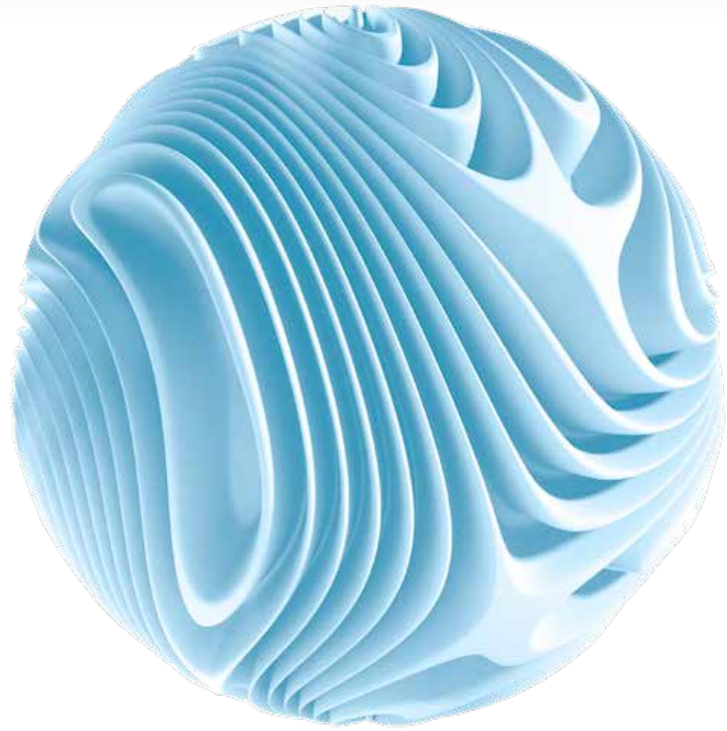


BioSkryb GENOMICS

# Application Areas

## BioSkryb core technology supports a broad range of single-cell and ultra-low input applications

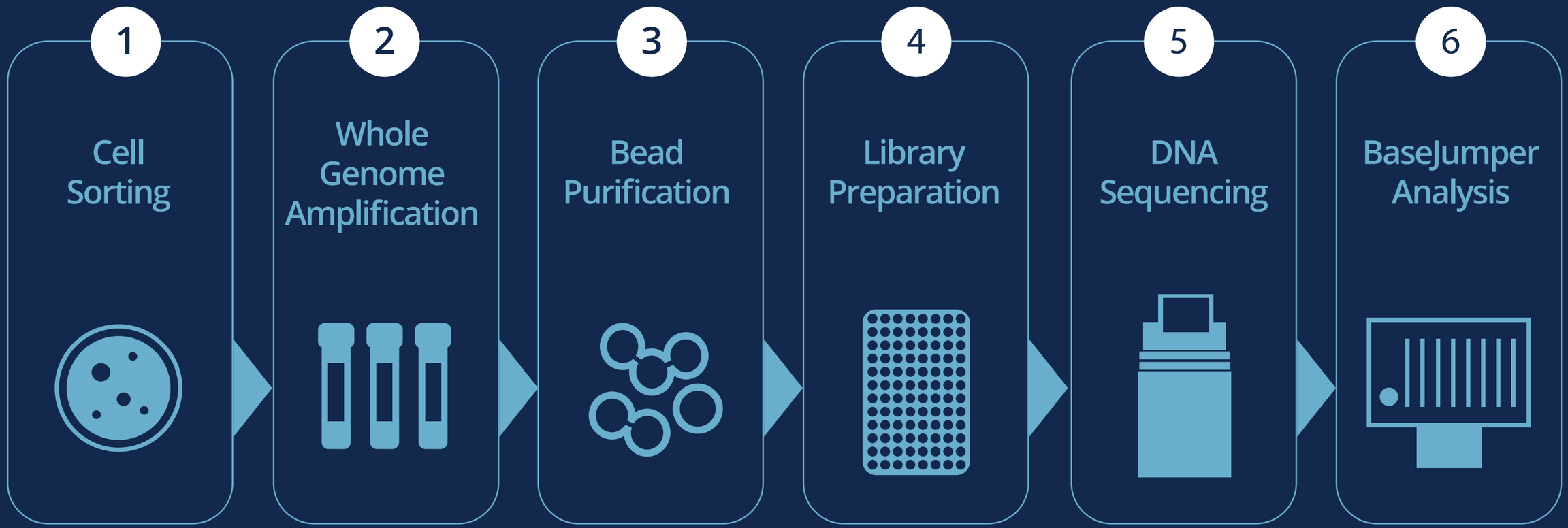
- Cancer genomics
- Prenatal genetic testing (PGT)
- Cardiology
- Microbiome research
- Neurology
- Toxicology
- Immunology
- Bioprocessing



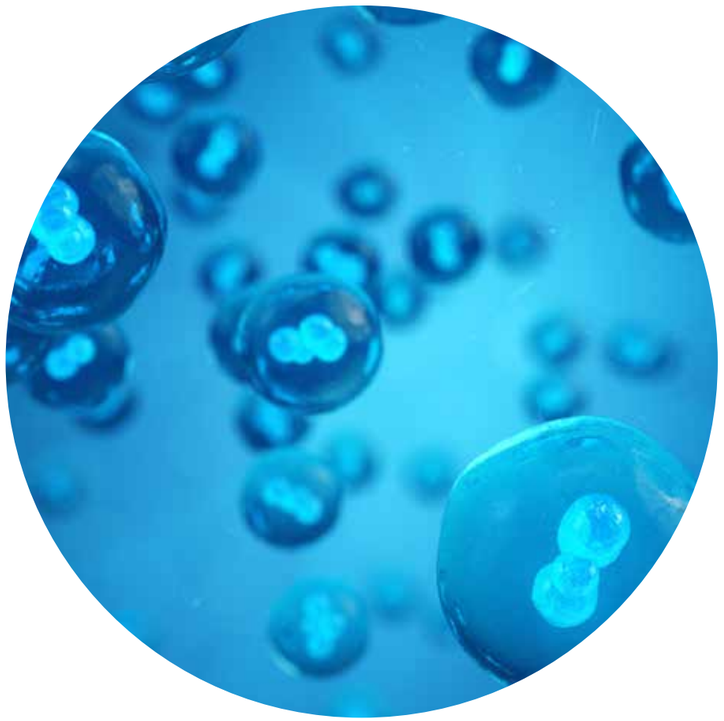
BioSkryb GENOMICS

# **ResolveDNA™** Whole Genome Sequencing Workflow

The ResolveDNA™ Whole Genome Sequencing Workflow is compatible with single cells, multiple cells and low-input (>4 pg to 10 ng) DNA samples. Whole genome amplification (WGA) is performed in three easy steps. WGA products are converted to libraries for Illumina® sequencing. The BaseJumper Bioinformatics Platform offers automated data processing and convenient visualization of variants.



# Cell Sorting



**The ResolveDNA™ Whole Genome Sequencing Workflow is compatible with fluorescence-activated cell sorting (FACS), as well as microfluidic and droplet-based cell sorting methods.**

The ResolveDNA™ FACS Kit contains 96-well plates and sealing film, as well as ResolveDNA PTA-Grade Cell Buffer—specifically optimized for PTA-based whole genome amplification from sorted cells.

FACS Kit components are also available as part of ResolveDNA Starter Packs. The Complete Starter Pack includes additional validated reagents, consumables and equipment for the ResolveDNA Whole Genome Sequencing Workflow. A Consumables Only Starter Pack is also available.

Product Details >

BioSkryb GENOMICS

# Whole Genome Amplification

FEATURES & BENEFITS

Product Details >

**ResolveDNA™ Whole Genome Amplification Kits overcome the inherent challenges of low coverage uniformity in single-cell genomics that lead to increased sequencing costs and complex data analysis.**

The controlled reaction parameters employed in this PTA-based kit enables reproducible recovery of >95% of the genomes of single cells and limited DNA input samples with industry-leading uniformity and accuracy.

Key features and benefits of ResolveDNA Whole Genome Amplification Kits include:

- Complete genomic coverage with bulk sample quality from a single cell
- Significantly lower allelic dropout and biases compared to existing WGA methods that yield low and variable coverage across the genome
- Specific amplification of the primary template with >97% of reads mapping to the human genome
- Low-cost, scalable approach to WGA with up to 384 reactions per kit
- Simple, user-friendly workflow that requires less than 30 mins of hands-on time and can be set up with automation

BioSkryb GENOMICS

# Whole Genome Amplification

WORKFLOW

## Designed for Ease of Use

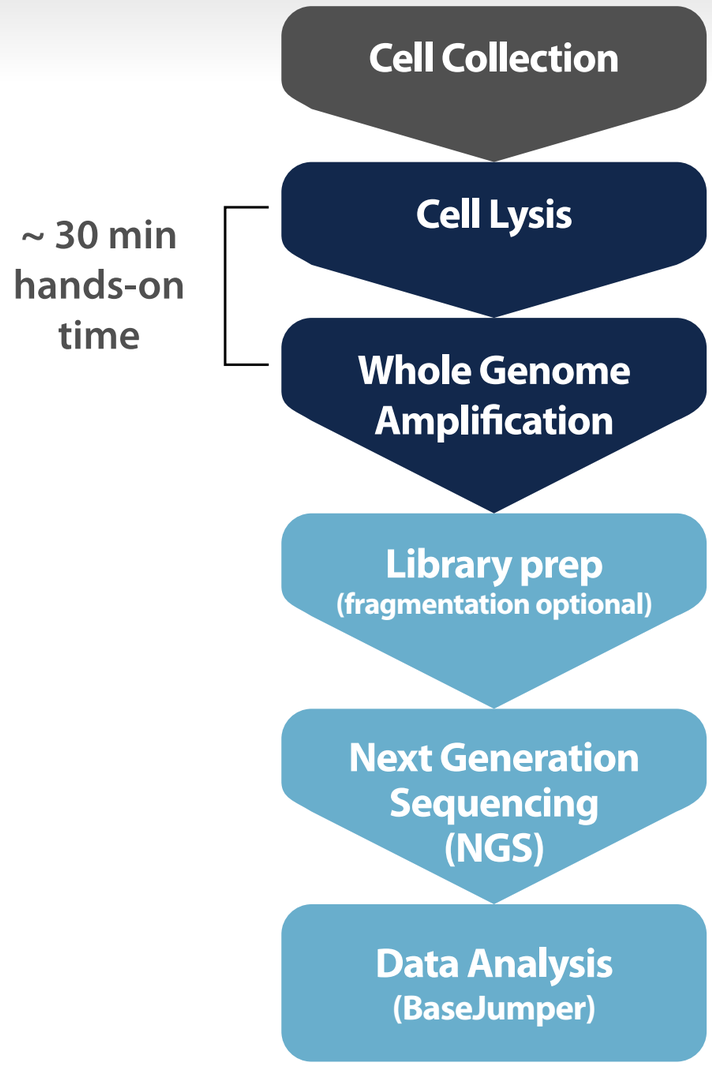
- Simple, user-friendly workflow that requires less than 30 mins of hands-on time

- Method consists of only two steps: cell lysis followed by whole-genome amplification

- An 8-hr, starting material to NGS run workflow

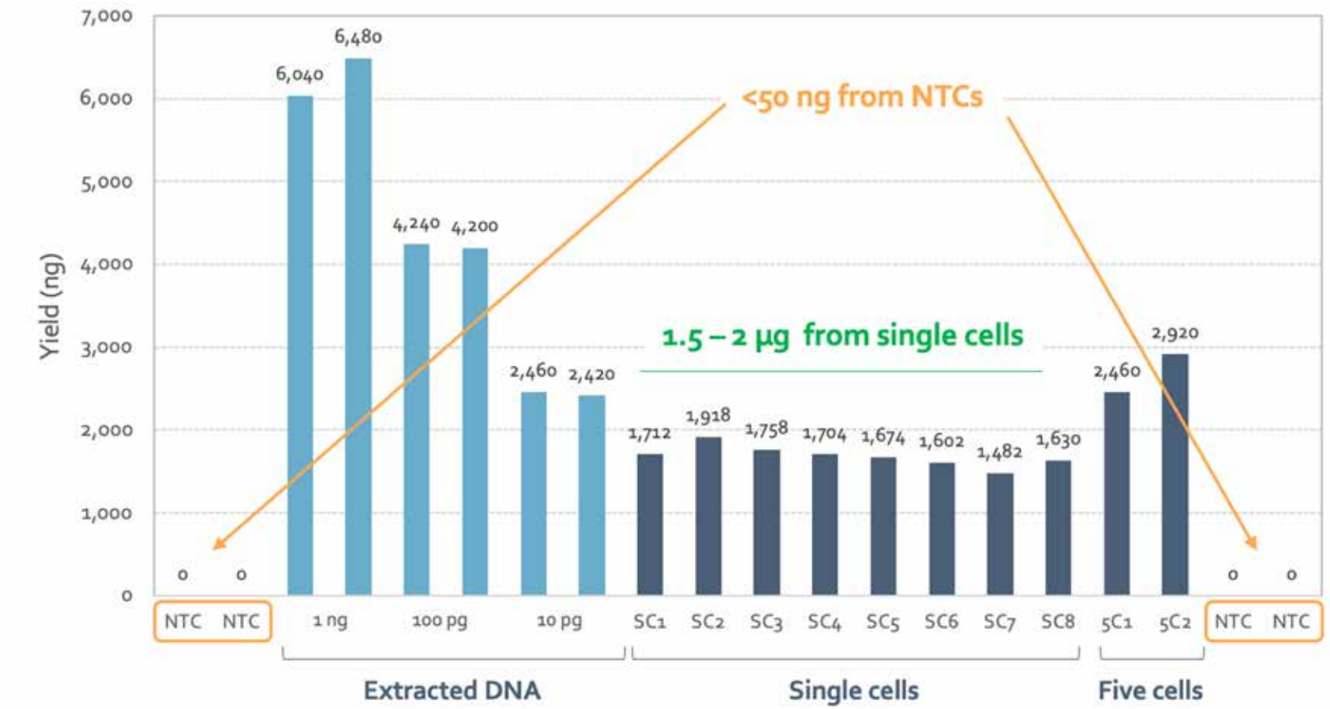
- Compatible with all known library prep approaches

- Optimized for both automated and manual reaction set-up



# Whole Genome Amplification

## LIBRARY QC METRICS



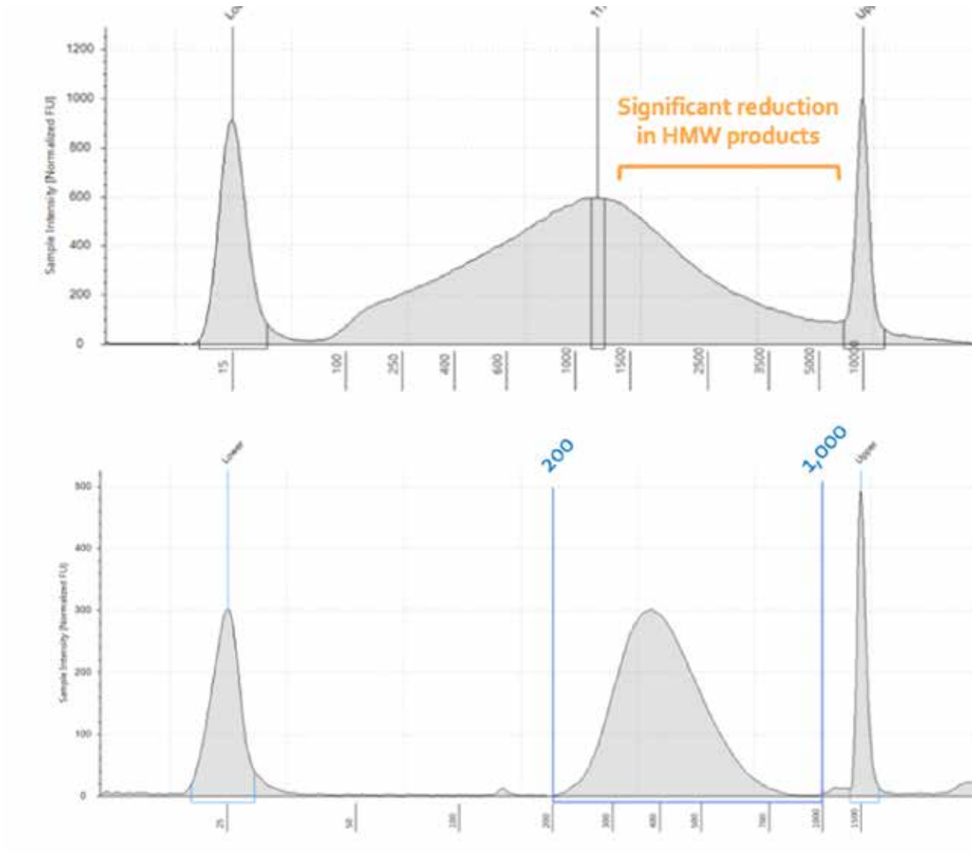

**ResolveDNA™ Whole Genome Amplification Kits offer consistent, low-microgram yields from single cell inputs.**

This enables robust library prep workflows, and allows for repeat analysis from the same sample. Reproducible, low-nanogram yields from no template controls (NTCs) confirm that only the product of interest is amplified.

BioSkryb GENOMICS

# Whole Genome Amplification

LIBRARY QC METRICS



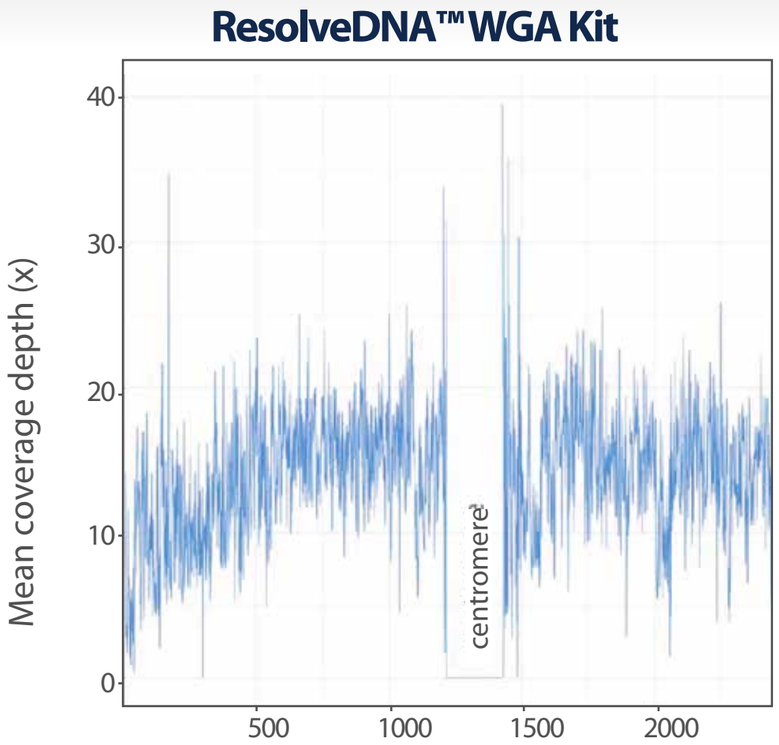

**ResolveDNA™ Whole Genome Amplification Kits enable control over fragment size.**

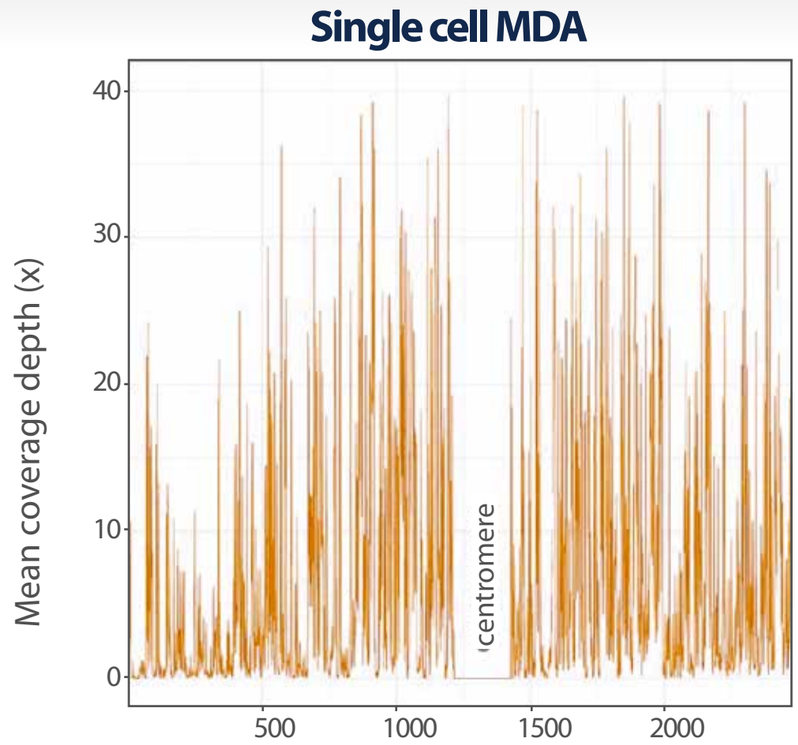
Unlike other WGA methods, the innovative PTA chemistry and quasi-linear isothermal process prevents amplification of daughter amplicons. This results in relatively short (~250 bp to >1.5 kb) reaction products. No fragmentation is required prior to library preparation, but bead-based size selection after library amplification may be used to obtain the optimal library insert size for your sequencing read length/application.

BioSkryb GENOMICS

# Whole Genome Amplification

SEQUENCING PERFORMANCE




**ResolveDNA Whole Genome Amplification Kits offer superior coverage and uniformity in single cell WGS.**
WGA was performed with the ResolveDNA WGA Kit (left) or single cell MDA (right). Plots show a portion of chromosome 1 (100 kb bins). The central area (poorly covered with both methods) corresponds to the centromere.

BioSkryb GENOMICS

# Whole Genome Amplification

SEQUENCING PERFORMANCE

| Method | ResolveDNA | Mixed Method A | MDA A | MDA B | Mixed Method B | Mixed Method C | DOP-PCR |
|---|---|---|---|---|---|---|---|
| Genome mapping | 97% | 91% | 88% | 55% | 88% | 55% | 52% |
| Genome recovery | 97% | 73% | 65% | 59% | 50% | 33% | 20% |
| CV of coverage | 0.8 | 1.3 | 1.8 | 2.3 | 2.6 | 3.2 | 3.6 |
| SNV sensitivity | 92% | 70% | 65% | 55% | 45% | 30% | 19% |
| SNV specificity | 99% | 88% | 87% | 88% | 28% | 35% | 35% |

Sensitivity and specificity are based on positions that are 15X coverage *SNV sensitivity for ResolveDNA approaches 85% at 30X coverage.
CV: Coefficient of Variation SNV: Single Nucleotide Variation

## ResolveDNA™ Whole Genome Amplification Kits offer superior coverage and uniformity in single-cell WGS.

Ten single cells were isolated from a human B-lymphocyte cell culture (CEPH1463/NA12878/ GM12878 human genome reference standard). WGA was performed on individual cells, using the ResolveDNA Whole Genome Amplification Kit. WGA products were converted to indexed libraries and subjected to high-coverage whole genome sequencing (WGS) on the Illumina® platform. For the other WGA methods, low-pass WGS data (generated from individual BJ1 fibroblasts), were obtained from a previously published study (Chen, C. et al. Science 2017; 356: 189).

To achieve a fair comparison of the various WGA methods, raw data for all samples were aligned and pre-processed for variant calling using the same pipeline. All metrics shown in the table were generated from randomly subsampled BAM files (300 million reads per cell). Note that the metrics for all the methods other than the ResolveDNA kit are overestimates, due to the way in which data analysis was performed in the original study.

# Bead Purification


**The ResolveDNA™ Whole Genome Amplification and library preparation workflows include a number of bead-based purification steps. ResolveDNA Bead Purification Kits contain validated paramagnetic beads, as well as an optimized elution buffer to ensure highly efficient bead cleanups.**

The ResolveDNA Dual Volume Strip Tube Magnet and Magnetic Plate are available to support all bead-based cleanups in the ResolveDNA™ Whole Genome Sequencing Workflow, in either plate or strip tube-based format.

The ResolveDNA Dual Volume Strip Tube Magnet is compatible with 8 strip 0.2 mL PCR tubes. One side handles volumes of 50 µL – 0.2 mL and the other side 5 µL – 50 µL.

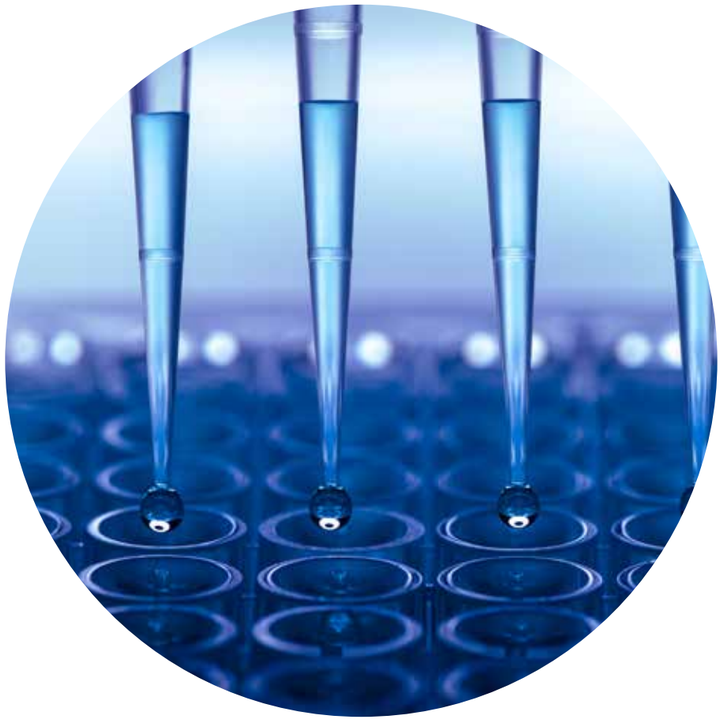

The ResolveDNA Magnetic Plate is compatible with full, semi and non-skirted PCR plates, and 0.2 mL PCR strips.

Product Details >

BioSkryb GENOMICS

# Library Preparation

OVERVIEW



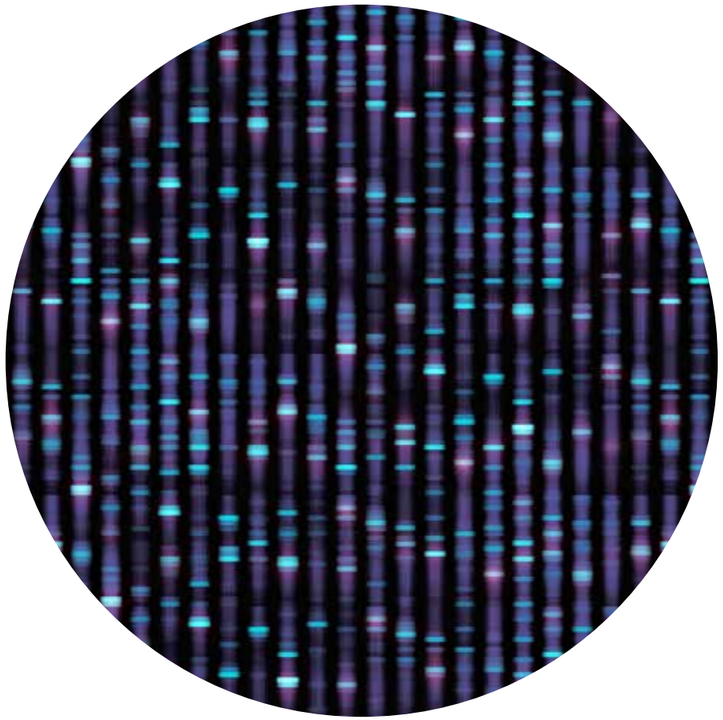
**To obtain superior whole genome sequencing data from single cells and ultra-low inputs, it is critical to preserve the quality of WGA reaction products generated with ResolveDNA™ WGA Kits during library preparation.**

ResolveDNA Library Prepration Kits employ proprietary technology and reagent formulations to retain molecular diversity and introduce minimal bias during the construction of sequencing-ready libraries. The streamlined, optimized, ligation-based workflow does not require fragmentation of input DNA (WGA reaction products). ResolveDNA Multi-Use Library Adapters are supplied in a convenient plate-based format. These full-length adapters provide unique dual indices compatible with all Illumina(R) sequencers.

Product Details >

BioSkryb GENOMICS

# Sequencing



**Appropriate experimental design is critical in single-cell genomics projects. Requirements may differ widely, depending on the application and study objectives.**

The total amount of sequencing required for a study is determined by the size of the cell population to be interrogated, as well as the desired sequencing depth. BioSkryb offers high-quality sequencing services to ensure that the valuable information contained in every cell is preserved every step of the way; from sample preparation to analysis. Our whole genome sequencing service includes an initial (optional) round of low-pass sequencing to assess library quality to ensure the most robust libraries move forward to deep sequencing.

Contact our experienced team for assistance with experimental design, highly competitive sequencing services, or customized projects, including whole genome amplification, library preparation, sequencing and/or analysis. We are here to help you explore, discover and transform.

Contact us >

BioSkryb GENOMICS

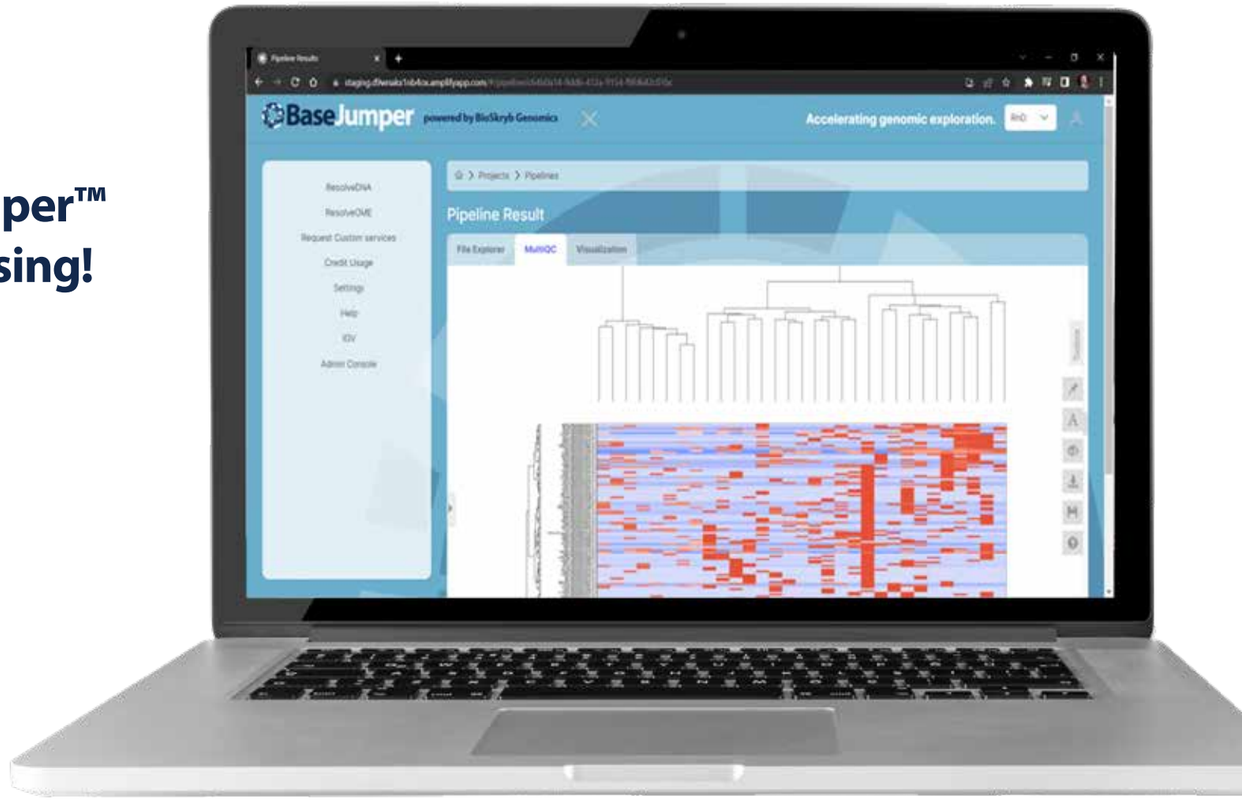
# Analysis

OVERVIEW

BaseJumper

## Accelerate genomic exploration today with the BaseJumper™ Bioinformatics platform. Discover what you've been missing!

- Cloud-based platform to accelerate single-cell informatics
- Single cell multiomics data analysis for both DNA and RNA
- Fast track the interpretation and visualization of large data sets
- Ultrafast filtering of millions of biomarkers in a study
- Generate publication-quality figures and reports




Contact us >

BioSkryb GENOMICS

# Analysis

SOLUTIONS

## The Mission

The BaseJumper™ Bioinformatics Platform, powered by BioSkryb Genomics, is designed to providebioinformatics analysis and interactive visualization at scale. Uncovering biomarkers and mechanisms of disease demands high volumes of complex data and the ability to quickly slice layers of analyses. Since multiomic (DNA, RNA, and Protein) data can be generated across a single cell, organization and mapping of the results are necessary to empower interplay of molecular features. BaseJumper™ brings speed and ease of use directly into the hands of its users, shifting time from computation to interpretation of results.

## The Answer - BaseJumper™

The BaseJumper platform provides a number of rich interactive visualizations, RNA/DNA analysis workflows and QC tools. With dynamic data filtering capabilities, researchers from all disciplines can accelerate the interpretation of results in common formats without deep expertise in computational and visual methods.

Contact us >

BioSkryb GENOMICS

# Analysis

## VISUALIZATION

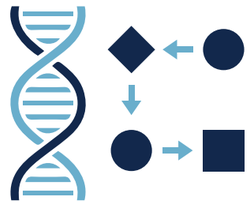
### A suite of visualization apps is available to users within the analysis project that can cover common areas of analysis such as:

- Genome browsing for allele changes and expression levels
- Cellular phenotype identification to colorize figures and drive significance analyses
- Sample grouping based on similarity of copy number, expression, genotype etc.
- Prevalence of genetic loci within copy aberrations across studies
- Expression-level views like heatmaps, PCAs and differential expression.
- Filtering of variants based on dozens of annotation databases and common genetic and cancer databases

Users create projects and organize data from their repositories of sequencing results and put through several pre-design bioinformatics workflows to derive a variety of biomarkers: variants (SNVs/ Indels), repetitive regions, copy number aberrations, structural variants, isoform variation, gene fusions, etc.

Access


Build



Compute

Display

Export

## Unlock the discovery potential from your single cell experiments with BaseJumper™ Bioinformatics

BioSkryb GENOMICS

# Single-Cell Multiomic Analysis

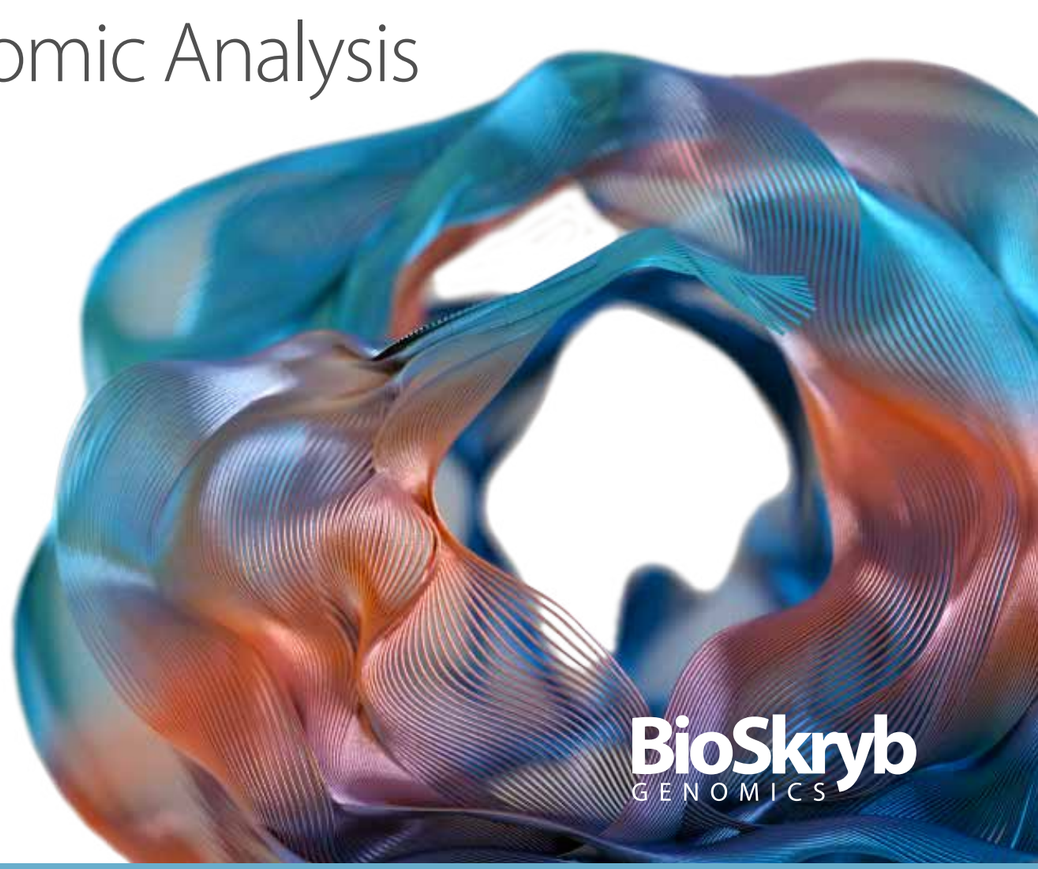
Introducing

# ResolveOME™

## Enabling Comprehensive Single-Cell Multiomic Analysis

BioSkryb's ResolveOME Whole Genome and Transcriptome Amplification Kit 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, our(the) ResolveOME Kit 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.

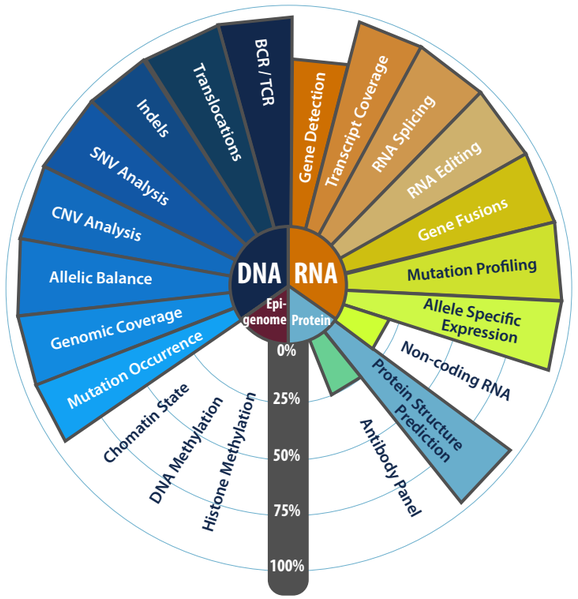
Product Details >



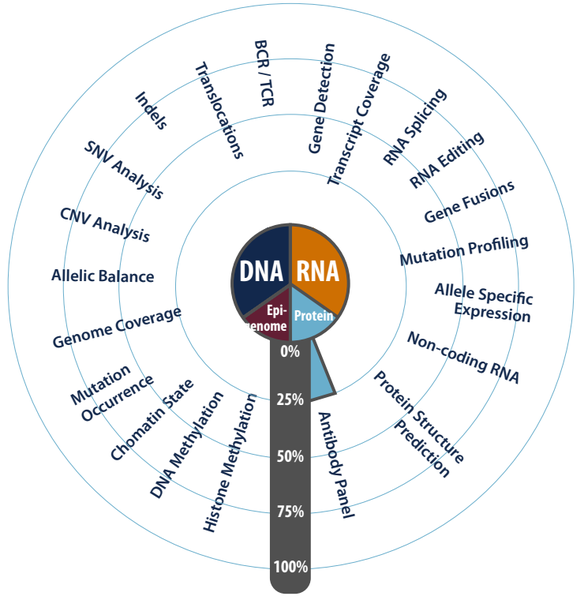
# Single-Cell Multiomic Analysis

DATA

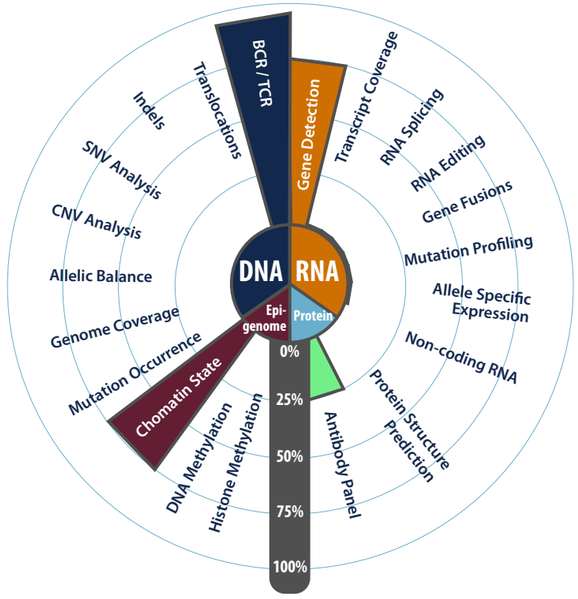
## ResolveOME




## Droplet DNA-seq




## Droplet RNA-seq




**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 Kit 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, our ResolveOME Kit yields 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.

# Single-Cell Multiomic Analysis

RESOLVEOME™ WHOLE GENOME AND TRANSCRIPTOME SEQUENCING WORKFLOW

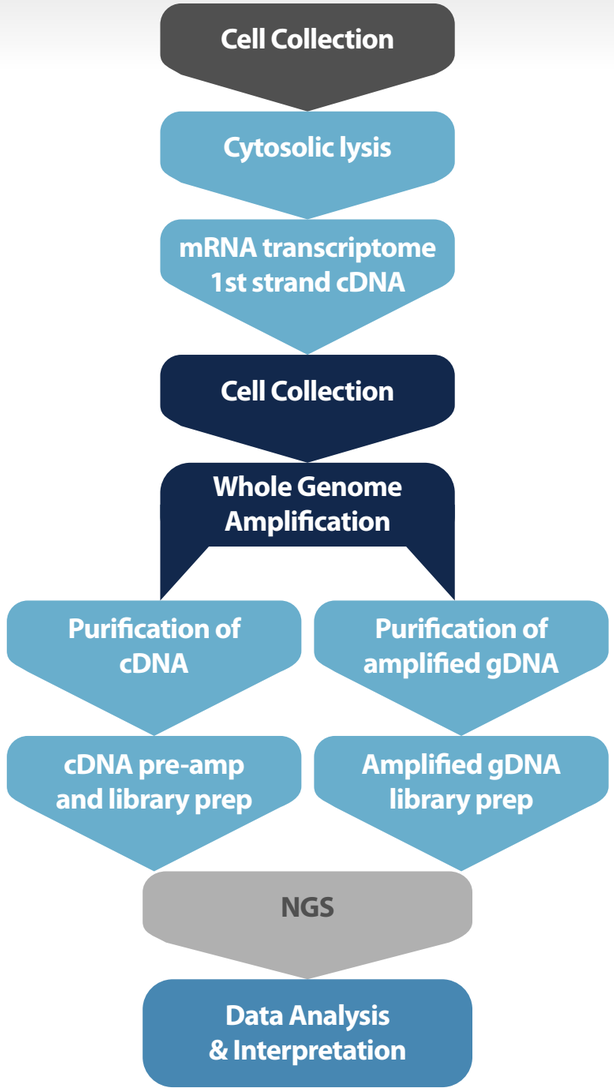
## Integrated ResolveOME workflow.

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.

- Only requires a single cell for the construction of a whole-genome and full-length mRNA transcriptome library, but it is compatible with bulk sample inputs.

- Completed in 2 – 3 days, from cell sorting to sequencing-ready libraries, with less than 9 hours of hands-on time.

- 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



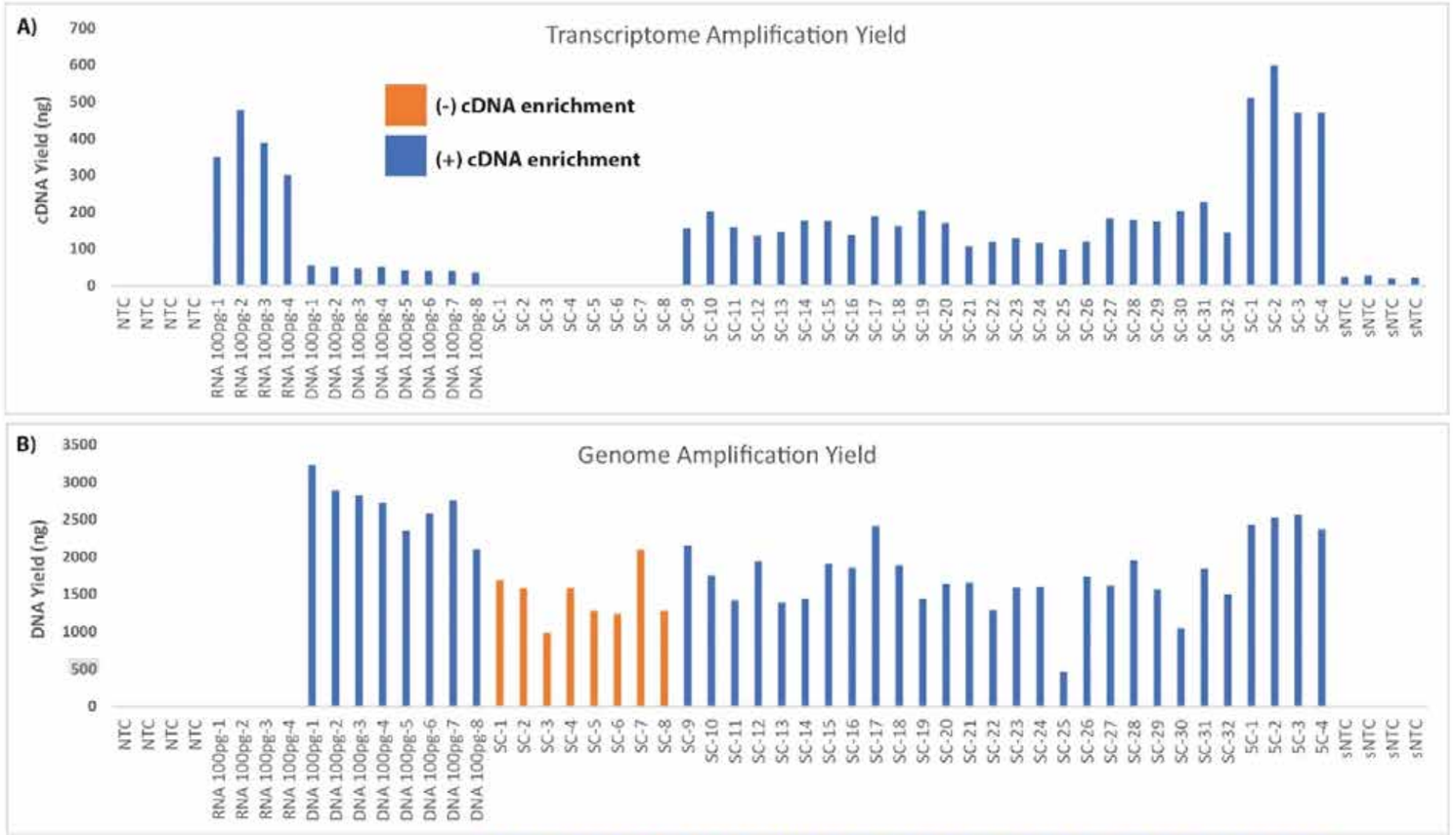
# Single-Cell Multiomic Analysis

## RESOLVEOME™ WHOLE GENOME AND TRANSCRIPTOME SEQUENCING WORKFLOW

- 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.

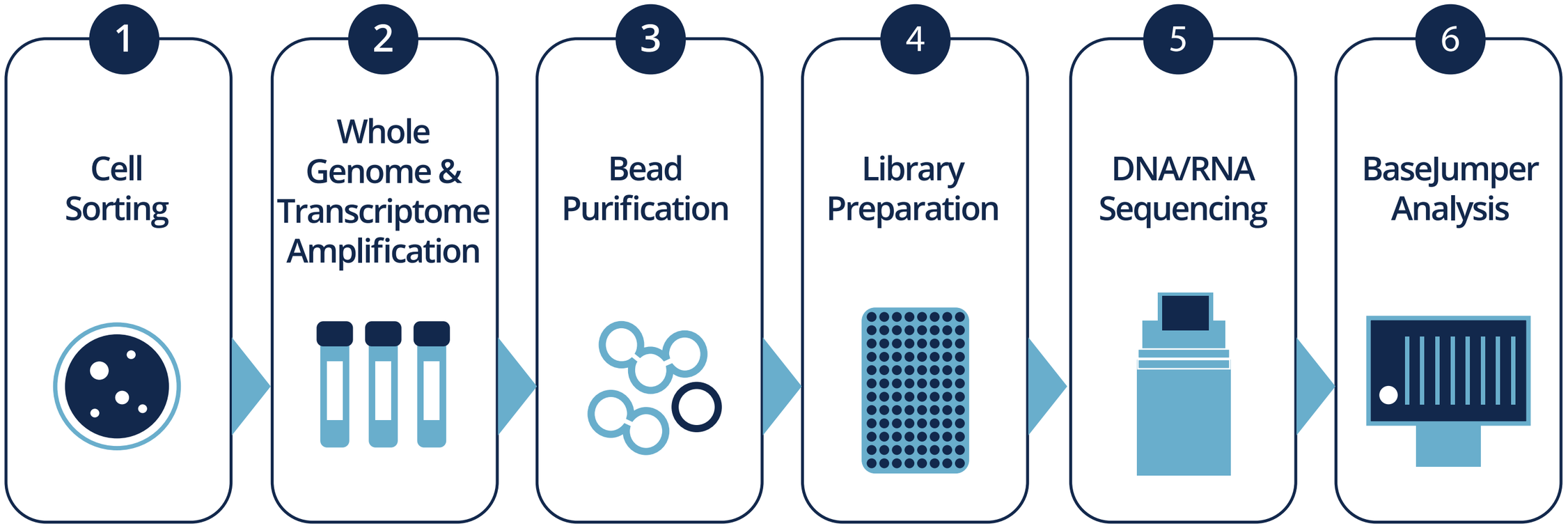
- Full transcriptome workflow enables enhanced RNA analysis compared to droplet-based single-cell RNA sequencing, providing full transcript RNA-Seq, splicing and isoform detection, and gene fusion detection.



# Single-Cell Multiomic Analysis

## RESOLVEOME™ WHOLE GENOME AND TRANSCRIPTOME SEQUENCING WORKFLOW

The ResolveOME™ Whole Genome and Transcriptome Sequencing Workflow is performed in a simple, efficient workflow. Products can be conveniently converted to libraries for Illumina® DNA sequencing. The BaseJumper Bioinformatics Platform uses standardized best practices for bioinformatic DNA sequencing analysis and offers automated data processing and convenient visualization of variants.



# Ordering Information

## STARTER PACKS & EQUIPMENT

**Please contact us to request a quote or to speak to a member of our team. info@bioskryb.com**

| | PRODUCT CODE | PRODUCT DETAILS | DESCRIPTION | PACK SIZE |
|---|---|---|---|---|
|  | **100137** | **ResolveDNA™ Complete Starter Pack:** | Everything needed to run PTA from start to finish. Each high-quality product in the ResolveDNA Complete Starter Pack has been carefully developed to provide optimal performance for the ResolveDNA Whole Genome Amplification Kit. | **Bundle** |
| | | ResolveDNA™ Whole Genome Amplification Kit | | 1 |
| | | ResolveDNA™ Library Preparation Kit | | 1 |
| | | ResolveDNA™ Multi-Use Library Adapters | | Pack of 25 |
| | | BioSkryb PCR Plate Spinner | | 1 |
| | | BioSkryb PCR Plate Thermal Mixer | | 1 |
| | | BioSkryb PCR Cooler | | 1 |
| | | BioSkryb Low Bind 96-well PCR Plates | | Pack of 25 |
| | | PCR Plate Sealing Film | | Pack of 100 |
| | | ResolveDNA™ PTA-Grade Cell Buffer Pack | | 12 x 500 µL |
| | | ResolveDNA™ Bead Purification Kit | | 96 reactions |
| | | ResolveDNA™ Magnetic Plate | | 1 |
|  | **100180** | **ResolveDNA™ Consumables Only Starter Pack:** | The ResolveDNA Consumables Only Starter Pack includes consumables needed for optimal results with your ResolveDNA Whole Genome Amplification Kit. | **Bundle** |
| | | ResolveDNA™ Whole Genome Amplification Kit | | Pack of 25 |
| | | ResolveDNA™ Bead Purification Kit | | 12 x 500 µL |
| | | ResolveDNA™ Library Preparation Kit | | Pack of 100 |
| | | ResolveDNA™ Multi-Use Library Adapters | | |
| | | BioSkryb Low Bind 96-well PCR Plates | | |
| | | ResolveDNA™ PTA-Grade Cell Buffer Pack | | |
| | | PCR Plate Sealing Film | | |

# Ordering Information

## STARTER PACKS & EQUIPMENT

| | PRODUCT CODE | PRODUCT DETAILS | DESCRIPTION | PACK SIZE |
|---|---|---|---|---|
|  | **100199** | **ResolveDNA™ FACS Kit:**<br>ResolveDNA™ PTA-Grade Cell Buffer<br>BioSkryb Low Bind 96-well PCR Plates<br>PCR Plate Sealing Film | The ResolveDNA FACS Kit contains 96-well plates and sealing film, as well as ResolveDNA PTA-Grade Cell Buffer—specifically optimized for PTA-based whole genome amplification from sorted cells. | **Bundle**<br>6 mL<br>Pack of 25<br>Pack of 100 |
|  | **100150** | **BioSkryb PCR Plate Thermal Mixer** | The BioSkryb PCR Plate Thermal Mixer, controlled by a DC brushless motor and microcomputer, perfectly combines the constant temperature and shaking required during the PTA process, optimizing time and improving efficiency. | Each |
|  | **100153** | **BioSkryb PCR Plate Spinner** | A high-quality plate spinner is required for quick spins throughout the PTA process. Designed for small samples in 96 or 384-well skirted, non-skirted and semi-skirted style plates. | Each |

BioSkryb GENOMICS

# Ordering Information

## WHOLE GENOME AMPLICATION KITS / WHOLE GENOME AND TRANSCRIPTOME AMPLIFICATION SYSTEM

| | PRODUCT CODE | PRODUCT DETAILS | DESCRIPTION | PACK SIZE |
|---|---|---|---|---|
|  | **100545** | **ResolveDNA™ Whole Genome Amplification Kit** | PTA-based kit for accurate and reproducible whole genome amplification from single cells and ultra-low-input DNA inputs (4 pg to <10 ng). | 1 Kit |
|  | **100500** | **ResolveOME™ Whole Genome and Transcriptome Amplification System** | PTA-based kit for accurate and reproducable whole genome and transcriptome amplification | 1 Kit |

BioSkryb GENOMICS

# Ordering Information

## BEAD PURIFICATION KITS AND MAGNETS

| | PRODUCT CODE | PRODUCT DETAILS | DESCRIPTION | PACK SIZE |
|---|---|---|---|---|
|  | **100182** | **ResolveDNA™ Bead Purification Kit** | For reliable cleanup of WGA reaction products and libraries prepared for Illumina® sequencing. | 96 reactions |
|  | **100135** | **ResolveDNA™ Magnetic Plate*** | Compatible with full-skirted, semi-skirted and non-skirted PCR plates and 0.2 mL PCR strip tubes. | Each |
|  | **100226** | **ResolveDNA™ Dual Volume Strip Tube Magnet** | Compatible with 8-strip 0.2 mL PCR tubes. Use one side of the magnet for volumes from 5 µL – 50 µL, and the other side for 50 µL – 0.2 mL volumes. | Each |

BioSkryb GENOMICS

# Ordering Information

## LIBRARY PREPARATION REAGENTS

**Please contact us to request a quote or to speak to a member of our team. info@bioskryb.com**

| | PRODUCT CODE | PRODUCT DETAILS | DESCRIPTION | PACK SIZE |
|---|---|---|---|---|
|  | **100080** | **ResolveDNA™ Library Preparation Kit** | Optimized ligation-based (without fragmentation) conversion of PTA products to Illumina®-ready libraries for sequencing. | 96 reactions |
|  | **100181** | **ResolveDNA™ Multi-Use Library Adapters** | Unique dual-indexed adapters compatible with all Illumina® sequencers. Compatible with the ResolveDNA™ Whole Genome Amplification Kit at a 10x dilution, allowing for multiple uses per adapter plate. | 960 Reactions |

**bioskryb.com**

All data on file.
For Research Use Only. Not for use in diagnostic procedures.
BIOSKRYB, RESOLVEDNA and BASEJUMPER are trademarks of BioSkryb, Inc.
All other product names and trademarks are the property of their respective owners.



BioSkryb GENOMICS