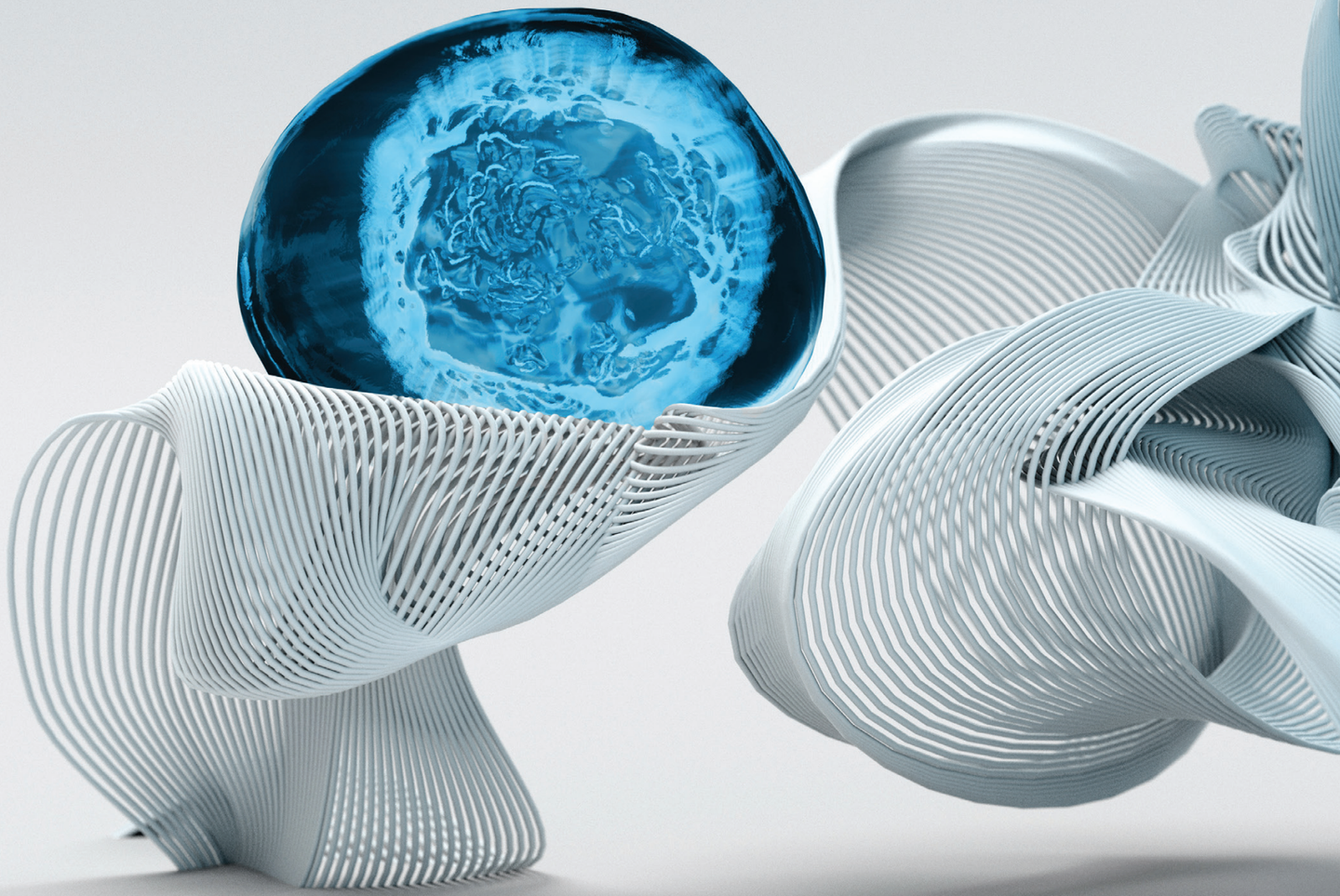
# A revolution in resolution

NOW AVAILABLE COMMERCIALLY

## ResolveDNA™

### Whole genome sequencing solution



BioSkryb GENOMICS

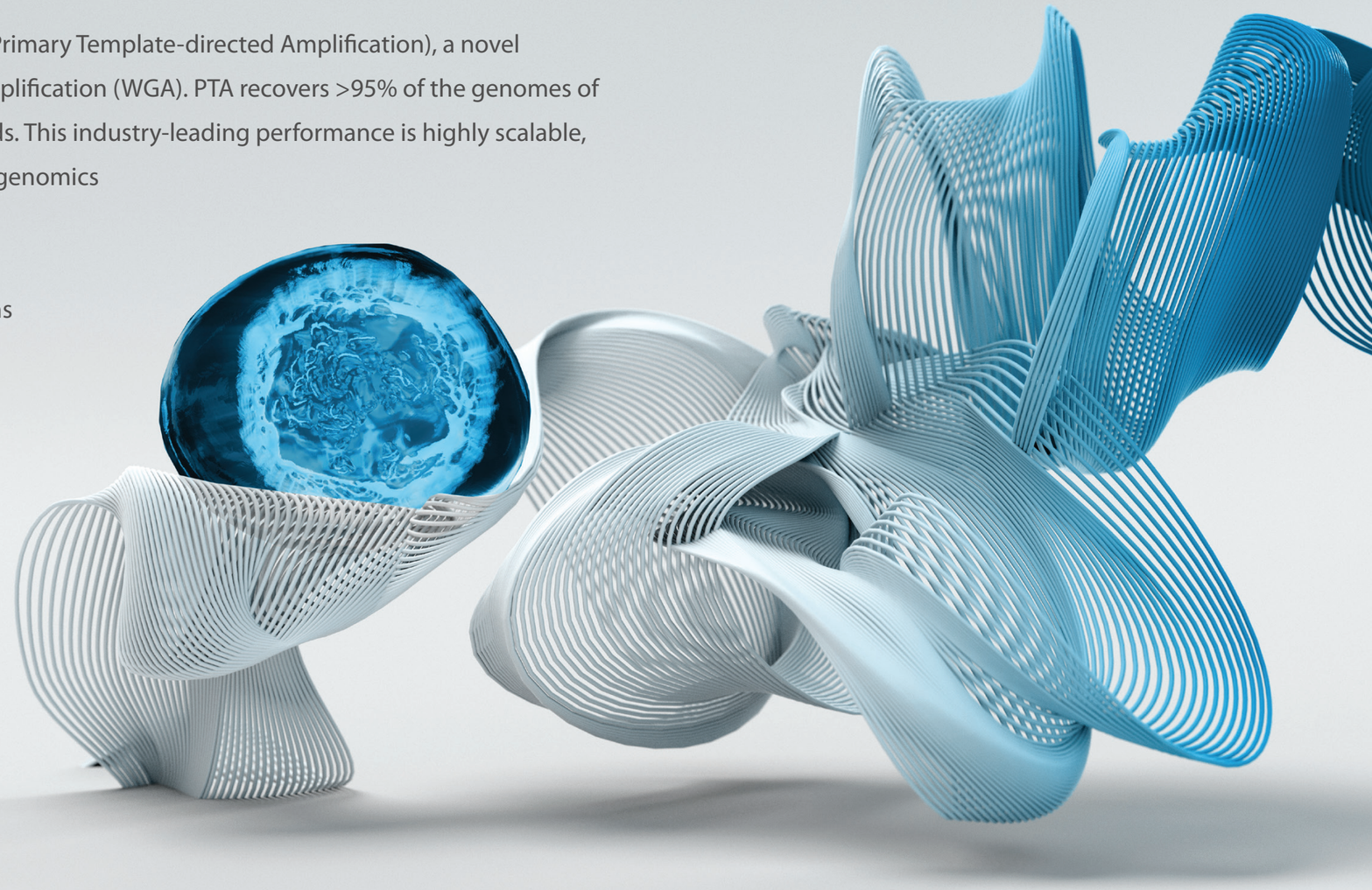
Cells explored. Answers revealed.

# 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.



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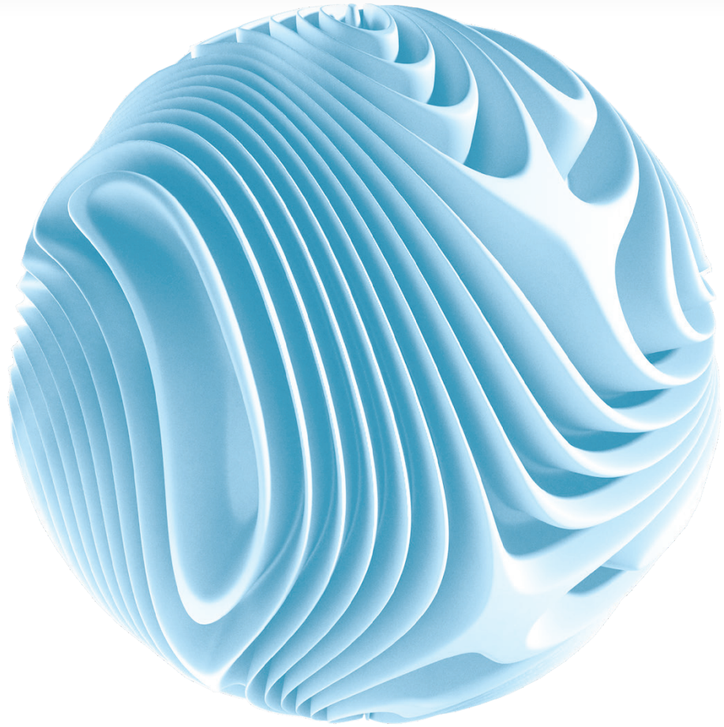
# Application Areas

## 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



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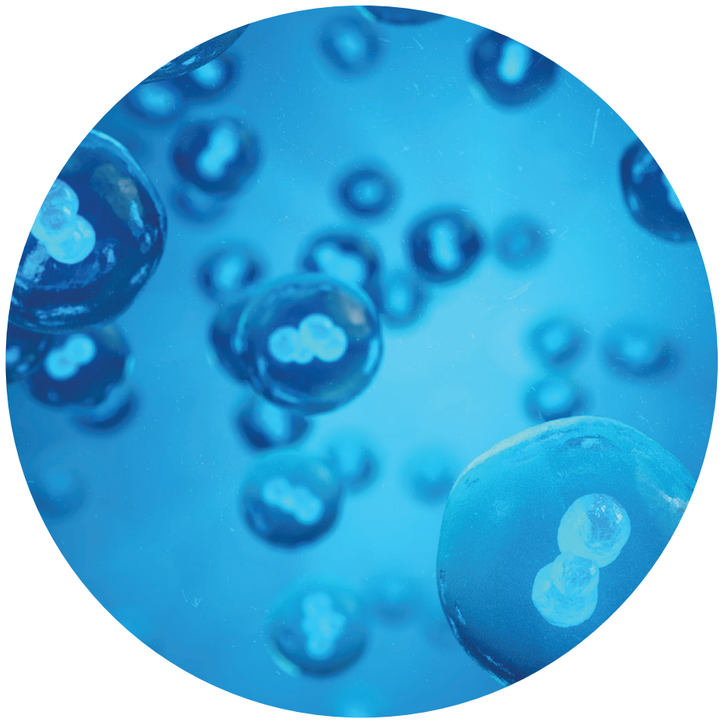
# **ResolveDNA™** Whole Genome Sequencing Workflow

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.

1. Cell Sorting
2. Whole Genome Amplification
3. Bead Purification
4. Library Preparation
5. DNA Sequencing
6. BaseJumper Analysis

# 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 >

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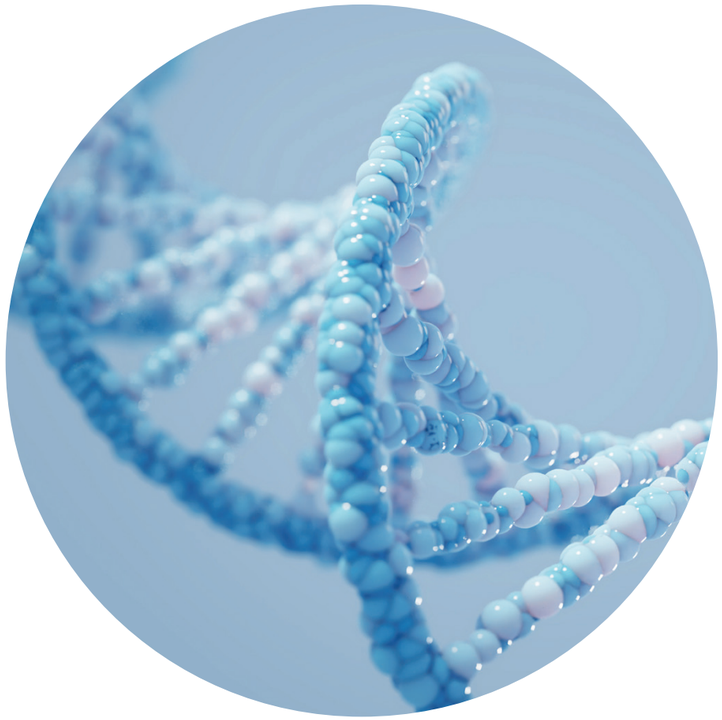
# Whole Genome Amplification

FEATURES & BENEFITS



**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:

- 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 and no detectable product in no template control reactions
- Simple, user-friendly workflow that requires less than 45 mins of hands-on time
- Consistent WGA fragment sizes and yields from picogram to nanogram inputs

Product Details >

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# Whole Genome Amplification

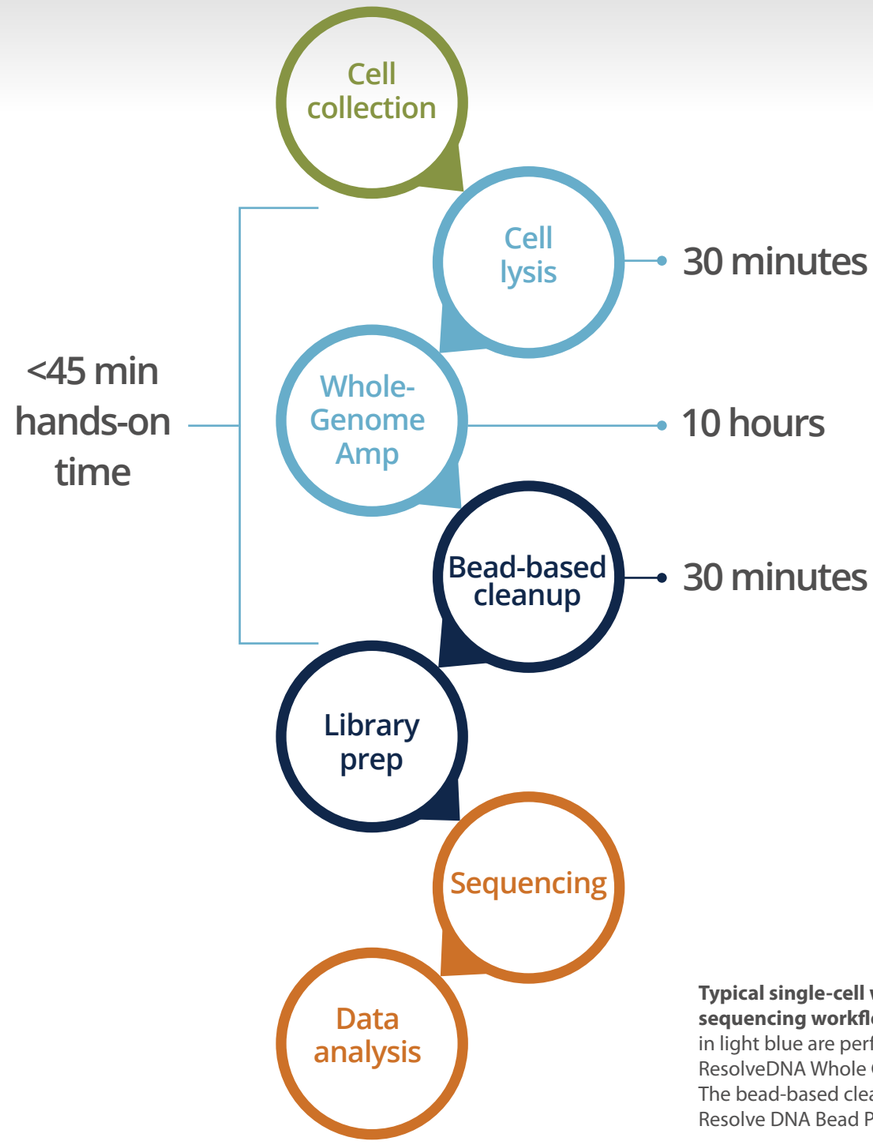
WORKFLOW

**Compatible with:**

- Single or multiple cells; ultra-low amounts of DNA (>4 pg—10 ng)
- Any cell collection method, plate or tube format

**Three easy steps:** cell lysis, whole genome amplification, bead-based cleanup of amplified DNA

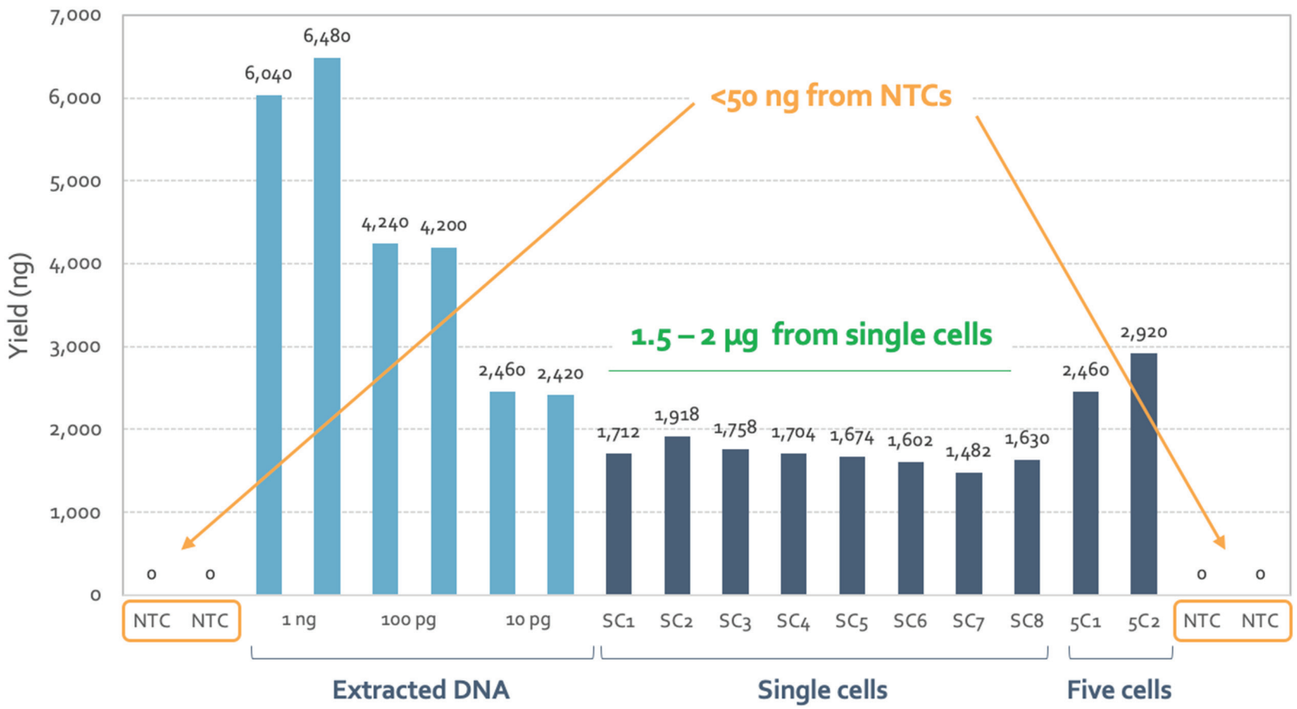
WGA products are converted to libraries for **multiplexed Illumina® sequencing** (no fragmentation required)




**Typical single-cell whole genome sequencing workflow.** Steps highlighted in light blue are performed with the ResolveDNA Whole Genome Amplification Kit. The bead-based cleanup is performed with the Resolve DNA Bead Purification Kit.

# 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.

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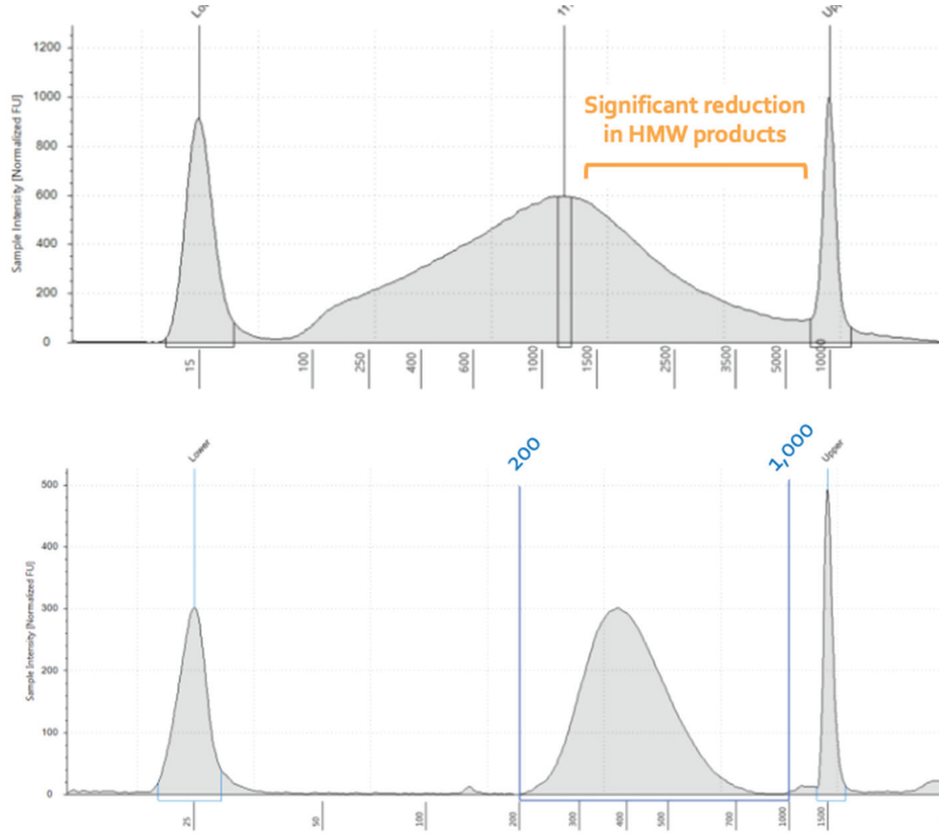
# Whole Genome Amplification

## 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.

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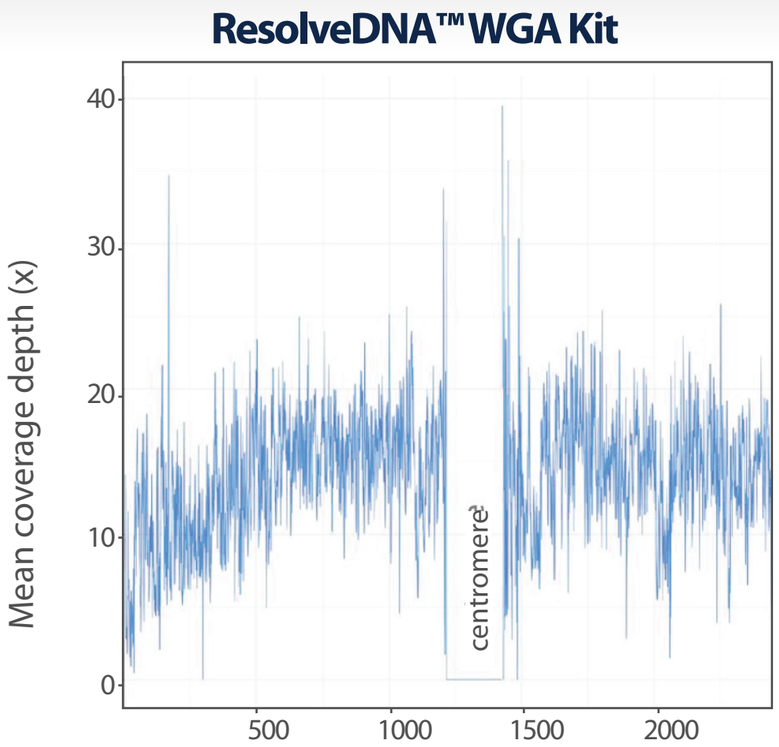
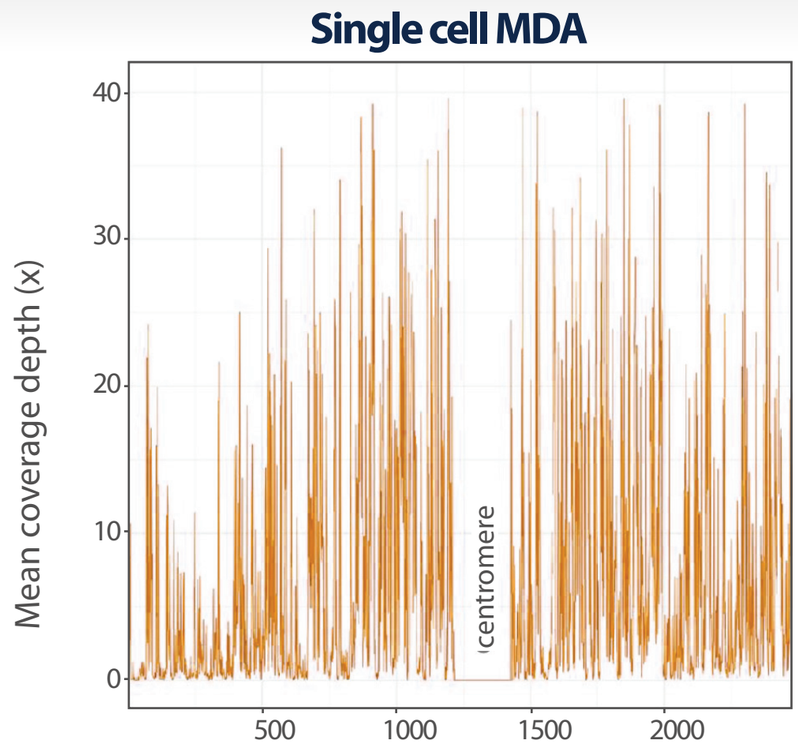
# Whole Genome Amplification

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.

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# 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 | 76%* | 38% | 40% | 35% | 25% | 10% | 4% |
| SNV specificity | 94% | 92% | 93% | 92% | 57% | 65% | 44% |

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 >

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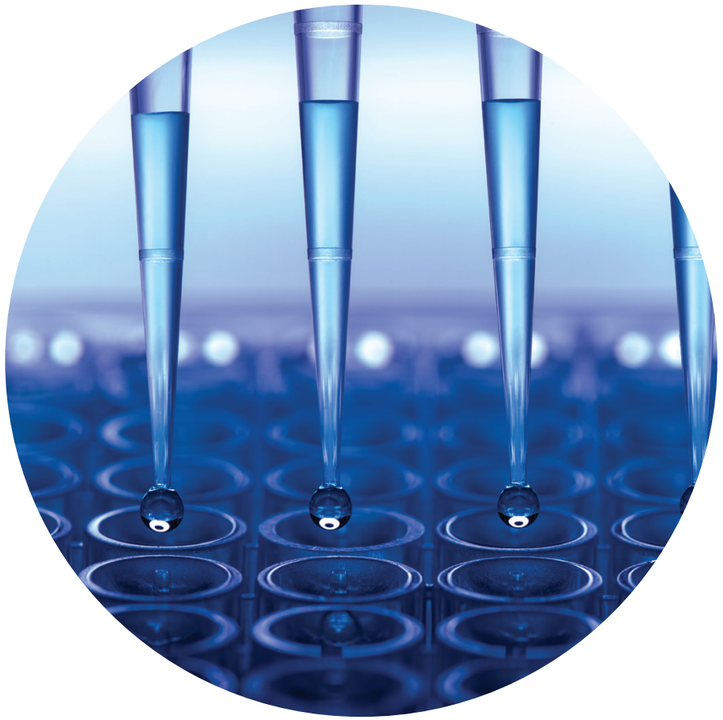
# Library Preparation

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 >

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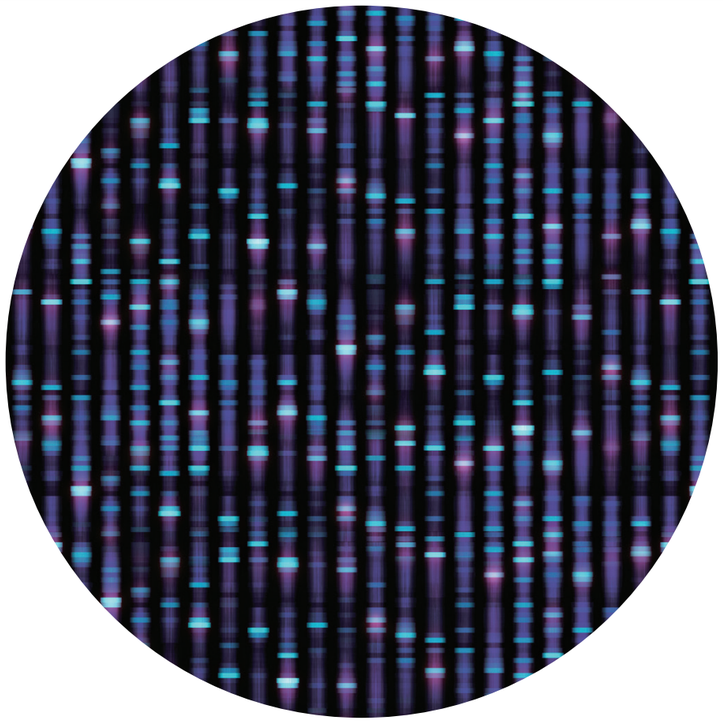
# Sequencing



**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 >

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# Analysis

OVERVIEW

## BaseJumper

**In addition to premium products and services, BioSkryb also offers innovative computational tools for analyzing human cells.**

The cloud-based BaseJumper Bioinformatics Platform was developed to significantly shorten the time between data generation and insights.

The platform uses standardized best practices for sequencing analysis, and enables biologists (with no bioinformatics expertise) to explore the unique features of human single-cell data. Powerful visualization tools provide easy access to variant data, annotations, and quality metrics across multiple cells. Aligned data may also be downloaded for exploration using other applications.


**Contact us to learn more about BaseJumper Bioinformatics Platform.**

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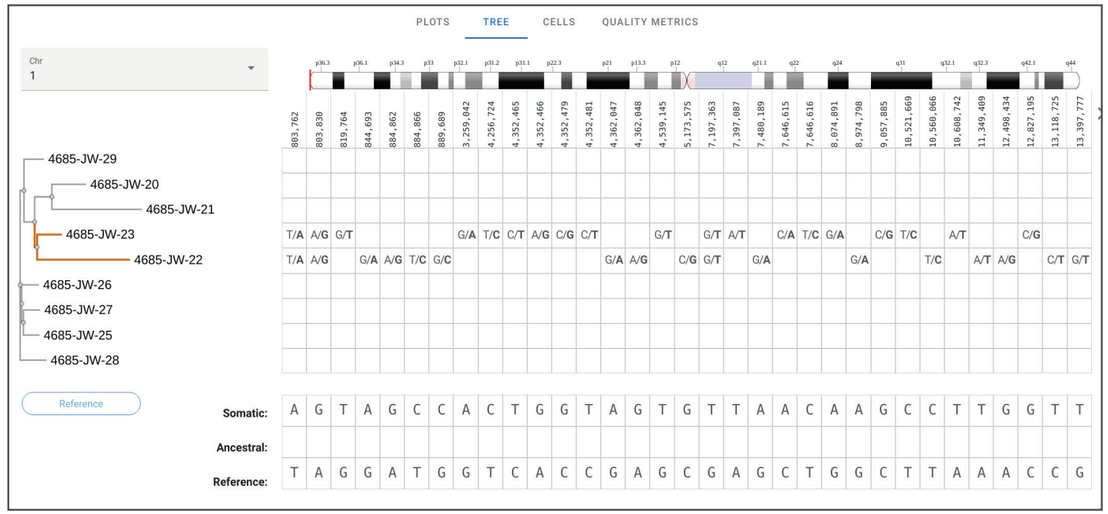
# Analysis

## VISUALIZATION TOOLS


**Circos plot** and IGV viewer show variant density across the genome. Variants can be filtered by several criteria, including origin (somatic vs germline), synonymous vs non-synonymous, or the presence of COSMIC annotations.




**Lineage browser** allows the exploration of variants that likely occurred ancestrally. Branches may be highlighted and explored at higher resolution, via built-in annotation and link-outs to additional annotation sources.

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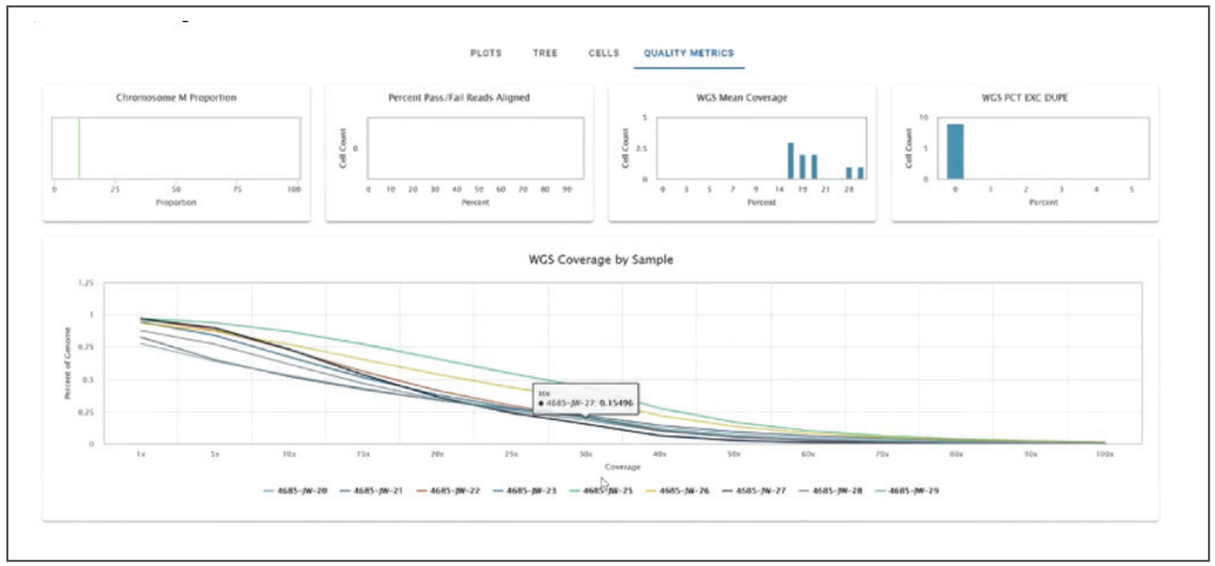
# Analysis

## VISUALIZATION TOOLS


**2D Cell** representation shows similarity of cells based on their somatic variants.




**Quality metrics** enables easy visualization of QC metrics for a data set.

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# 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:**<br>ResolveDNA™ Whole Genome Amplification Kit<br>ResolveDNA™ Library Preparation Kit<br>ResolveDNA™ Multi-Use Library Adapters<br>BioSkryb PCR Plate Spinner<br>BioSkryb PCR Plate Thermal Mixer<br>BioSkryb PCR Cooler<br>BioSkryb Low Bind 96-well PCR Plates<br>PCR Plate Sealing Film<br>ResolveDNA™ PTA-Grade Cell Buffer Pack<br>ResolveDNA™ Bead Purification Kit<br>ResolveDNA™ Magnetic Plate | 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**<br>96 reactions<br>96 reactions<br>960 Reactions<br>1<br>1<br>Pack of 25<br>Pack of 100<br>12 x 550 µL<br>96 reactions<br>1 |
|  | **100180** | **ResolveDNA™ Consumables Only Starter Pack:**<br>ResolveDNA™ Whole Genome Amplification Kit<br>ResolveDNA™ Bead Purification Kit<br>ResolveDNA™ Library Preparation Kit<br>ResolveDNA™ Multi-Use Library Adapters<br>BioSkryb Low Bind 96-well PCR Plates<br>ResolveDNA™ PTA-Grade Cell Buffer Pack<br>PCR Plate Sealing Film | The ResolveDNA Consumables Only Starter Pack includes consumables needed for optimal results with your ResolveDNA Whole Genome Amplification Kit. | **Bundle**<br>96 reactions<br>96 reactions<br>96 reactions<br>960 reactions<br>Pack of 25<br>12 x 550 µL<br>Pack of 100 |

# 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 |

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# Ordering Information

## WHOLE GENOME AMPLIFICATION KITS

| | PRODUCT CODE | PRODUCT DETAILS | DESCRIPTION | PACK SIZE |
|---|---|---|---|---|
|  | **100068** | **ResolveDNA™ Whole Genome Amplification Kit** | 24 reaction PTA-based kit for accurate and reproducible whole genome amplification from single cells and ultra-low-input DNA inputs (4 pg to <10 ng). | 24 reactions |
|  | **100136** | **ResolveDNA™ Whole Genome Amplification Kit** | 96 reaction PTA-based kit for accurate and reproducible whole genome amplification from single cells and ultra-low-input DNA inputs (4 pg to <10 ng). | 96 reactions |

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# Ordering Information

## BEAD PURIFICATION KITS AND MAGNETS

| | PRODUCT CODE | PRODUCT DETAILS | DESCRIPTION | PACK SIZE |
|---|---|---|---|---|
|  | **100121** | **ResolveDNA™ Bead Purification Kit** | For reliable cleanup of WGA reaction products and libraries prepared for Illumina® sequencing. | 24 reactions |
|  | **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 |

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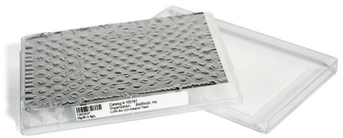
# Ordering Information

## 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 |

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