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Whole Genome Sequencing (WGS) for Therapeutic Cell Characterization

Whole genome sequencing, WGS, is a powerful approach for evaluating genomic integrity and supporting tumorigenicity risk assessment for therapeutic cells advancing toward clinical development. Avance Biosciences provides WGS services under CGMP/GLP-aligned workflows to support genome integrity assessment as a primary objective. Our WGS services are designed to identify both sequence-level variants and large-scale genomic abnormalities that may impact product safety, stability, and regulatory readiness.

Our Expertise

Our approach integrates complementary short-read and long-read sequencing to evaluate a broad range of genomic risk factors, from single-nucleotide variants to chromosomal-scale events. This combined strategy helps sponsors characterize therapeutic cells more comprehensively than short-read sequencing alone, particularly when structural rearrangements, copy number alterations, or complex integrations are a concern.

Genomic Integrity Assessment Across Cell Platforms

Platform	Descriptions
iPSC-derived Cell Therapies	Pluripotent stem cell–based products requiring careful genomic stability monitoring due to extended culture and differentiation processes.
Engineered T Cell Products	Genetically modified immune cell therapies, such as CAR-T or TCR-T, where insertional events and structural integrity must be assessed.
Gene-edited Cell Lines	CRISPR- or nuclease-edited cells requiring comprehensive on-target, off-target, and chromosomal integrity evaluation.

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Genomic Integrity Assessment Across Cell Platforms (Continued)

Platform	Descriptions
Stem cell–derived Products	Differentiated or expanded stem cell populations where prolonged culture may introduce genomic alterations.
Immortalized Production Cell Lines	Manufacturing cell substrates that require genomic characterization to ensure stability and safety.

Whole Genome Sequencing Services

Primary Capability	Platform/ Coverage	Deliverables
Genome-wide Variant Detection	• Short-read • Element AVITI • ≥ 50 x coverage	• Small nucleotide variants and small indels • Annotation against clinically relevant databases (e.g., ClinVar and COSMIC) to assess pathogenicity and cancer relevance of variants identified in tumor suppressor, oncogene, DNA repair, and cell cycle regulatory genes. • Variant classification where applicable
Detection of Large Insertions and Deletions	• Long-read • PacBio Vega • ≥ 15 x coverage	• Large insertions/deletions: inversions, translocations, complex rearrangements • Copy number alteration and aneuploidy assessment • Chromosomal integrity and genome architecture summary
Unbiased Integration Site Analysis	• Short-read and long-read with Element AVITI and PacBio Vega	• Detection of integration events • Characterization of integration structure and events (e.g., intact vs partial) • Annotation of off-target integration sites against clinically relevant gene databases as part of tumorigenicity and genomic stability safety assessment. • Detection of concatemers and tandem integration events.

Short-read Sequencing Workflow

Avance Biosciences offers validated (GMP) short-read Whole Genome Sequencing for comprehensive detection of single nucleotide polymorphisms (SNPs) and small insertions/deletions (Indels). Our workflow utilizes PCR-free high-quality library preparation, high-depth short-read sequencing (typically targeting ≥50× mean genome coverage for therapeutic-cell applications), validated bioinformatics analysis, and comprehensive variant annotation to provide high-confidence genomic characterization throughout product development.

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Short-read Sequencing Workflow (Continued)

Library Preparation and Sequencing	High-quality genomic DNA is extracted from submitted cell samples and assessed for purity and integrity prior to library preparation. Whole genome sequencing libraries are prepared using optimized protocols followed by library quality control and short-read sequencing. Sequencing depth is designed to provide robust SNP and small Indel detection, with therapeutic-cell projects typically performed at approximately 50× mean genome coverage.
Validated Bioinformatics Pipeline	The validated bioinformatics workflow transforms raw sequencing data into high-confidence SNP and small Indel variant calls using industry-standard analytical algorithms and rigorous quality control. The workflow maintains a complete electronic audit trail from sequencing data generation through bioinformatics analysis and reporting, and supports 21 CFR Part 11-compliant electronic records and data integrity requirements for GMP testing.
Assay Validation	The Avance Biosciences Whole Genome Sequencing assay has been validated using reference genomic materials. Validation evaluated the complete analytical workflow, including library preparation, sequencing, bioinformatics analysis, and variant calling, to demonstrate reliable SNP and small Indel detection. • Accuracy through comparison with established variants • Precision by reproducible SNP and Indel calls across replicate analyses • Reproducibility across independent sequencing runs • Analytical sensitivity for true SNP and small Indel detection • Analytical specificity by minimizing false-positive variant calls
Comprehensive Variant Annotation	Detected variants are annotated using established public genomic resources to provide: • Gene annotation • Functional consequence • Protein impact • Population allele frequency • Clinical significance, when available • Disease association • Computational prediction of functional impact
Deliverables	• Sequencing quality metrics • Genome coverage statistics • Summary of SNPs • Summary of small Indels • Annotated variant tables • Comparative analysis with reference/parental samples (optional) • VCF files (optional) • Comprehensive analytical report

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