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The KROMA**SURE**™ Platform

Assessing Genomic Structure and Genome Integrity in Cell and Gene Therapy

Executive Summary

Cell and gene therapies are defined not only by the specific genetic changes introduced by design, but by the genomic stability of the living cellular target or starting material, and the degree to which this critical attribute is maintained throughout modification and administration. The inherent biology of the target cells, including whether cells are expanded and engineered ex vivo or modified directly within the body, plays a central role in how genomic structure and genome integrity respond. Editing tools, viral and non-viral delivery systems, cell expansion, and differentiation all impose stress on the genome that is not fully captured by sequence-based analytical methods alone.

Disruptions to genomic structure, chromosome integrity, and genome integrity can arise naturally during cell growth or be increased by intrinsic cellular properties, process conditions, donor biology, or delivery modality, with implications for product consistency, clonal behavior, and long-term risk, with the current analytical toolkit being insufficient to capture these outcomes.

The KROMASURE™ platform was developed to address this gap. By combining advanced single cell cytogenetic analysis, expert interpretation, and scalable image-based analytics, KROMASURE provides a consistent framework for detecting, quantifying, and interpreting genome integrity risk across therapeutic modalities and biological contexts.

KROMASURE is a platform that integrates orthogonal single cell cytogenetic assays including K BAND™, SCREEN™, InSite™, and PinPoint™, enabling both whole genome and targeted assessment in dividing and non-dividing cells, providing actionable data beyond that of a single assay. Together with quantitative event burden analysis, benchmarking and threshold frameworks, and expert interpretation aligned to development and regulatory decision making, this comprehensive cytogenetic toolset provides cell and gene therapy developers with actionable insight into genomic structure, chromosome stability, and genome integrity across diverse biological contexts. Together, these elements support fit-for-purpose genome integrity assessment across allogeneic, autologous, and *in vivo* gene therapy programs.

WHY GENOME INTEGRITY AND GENOMIC STRUCTURE MATTER

Genomic Stability Reflects Replication and Repair Fidelity

Genomic integrity is not defined solely by DNA sequence accuracy at a target locus. It reflects a cell's ability to faithfully replicate its genome, preserve chromosome structure and copy number, and maintain stable genomic architecture across proliferation, differentiation, and cellular maintenance.

In cell and gene therapy development, replication and repair fidelity are routinely influenced by genome editing interventions, vector delivery, cell expansion, and differentiation. In many programs, these effects are further shaped by the intentional modulation of DNA repair and cell cycle pathways to promote on-target integration efficiency, homology-directed repair, or other desired outcomes. While these strategies are central to effective therapeutic engineering, they can also alter how genomes are copied, repaired, and maintained, making it essential to directly assess their impact on genomic structure and chromosome integrity in the final product.

Disruptions to replication fidelity or structural preservation can lead to the accumulation of abnormalities affecting genomic structure and chromosome integrity, including aneuploidy, large deletions, structural rearrangements, polyploidy, and complex events. These outcomes may influence cellular fitness, clonal behavior, long-term product consistency and safety, underscoring the importance of genome integrity assessment alongside editing efficiency.

The Limits of Sequence-Based Genomic Assessment

Sequence-based methods play a critical role in characterizing intended edits and small-scale variants. However, they provide an incomplete view of genome integrity when used in isolation. Large deletions, complex structural rearrangements, copy number changes, and balanced events are difficult to resolve using sequencing approaches alone, particularly when such events occur in a subset of cells rather than uniformly across a population.

In addition, population-averaged sequencing data can obscure cell-to-cell heterogeneity and cannot directly determine whether multiple structural events co-occur within the same cell. As a result, important information about how genomes are structurally maintained, or destabilized, during editing, expansion, and differentiation may be missed.

Direct assessment of genomic structure at the single-cell level provides the ground truth required for accurate interpretation of sequencing-based analyses and enables a more complete understanding of genome integrity risk.

Cytogenetic Analysis as a Foundation for Genome Integrity Decisions

Within the KROMASURE platform, cytogenetic analysis, which has long served as the foundation for assessing chromosome integrity, is preserved and extended through fit-for-purpose implementations designed specifically for cell and gene therapy development. Cytogenetic analysis has long served as the foundation for assessing chromosome integrity, providing direct visualization of chromosome structure, copy number, and large-scale rearrangements at the single-cell level.

Whole-genome cytogenetic assessment establishes the structural context to interpret targeted findings. By anchoring analysis in direct observation of genomic structure, KROMASURE ensures that targeted or high-throughput results are interpreted within the broader chromosomal landscape rather than in isolation.

This integrated approach allows developers to understand not only whether specific events occur, but how those events relate to overall genome integrity and population-level stability.

Event Burden as a Measure of Genome Integrity

KROMASURE applies quantitative event burden analysis to measure the frequency, distribution, and recurrence of abnormalities affecting genomic structure and chromosome integrity across a cell population. This approach enables differentiation between background variation and patterns more consistent with elevated genomic risk. Genome integrity is most effectively characterized as a population-level property rather than as a catalog of individual abnormalities. Low-frequency structural and numerical events may arise during normal cell proliferation, while elevated frequencies, recurrence across cells, or enrichment of specific event classes can indicate reduced replication fidelity or process-driven instability.

By focusing on event burden rather than isolated findings, developers gain a clearer understanding of how editing strategies, repair pathway modulation, and manufacturing conditions influence genome integrity over time.

The KROMASURE Platform

KROMASURE integrates a comprehensive set of single-cell cytogenetic solutions designed to provide both breadth and depth of insight into genome integrity.

Unbiased, chromosomal level analysis enables direct assessment of chromosome structure, copy number, and large-scale rearrangements across large numbers of dividing cells, supporting statistically robust evaluation of population-level stability. Targeted assays extend this capability to specific loci, edit sites, or transgene integration regions, with applicability to both dividing and non-dividing cells.

Together, these complementary approaches allow developers to select fit-for-purpose analytical depth based on biological context, therapeutic modality, and stage of development, while maintaining consistency within a unified interpretive framework.

KROMASURE™ Applications Across Therapeutic Modalities

ALLOGENEIC CELL THERAPIES

Allogeneic programs must account for donor-to-donor variability, editing-induced structural outcomes, and genomic changes introduced during expansion. KROMASURE supports baseline genome integrity assessment of starting material, comparison of editing and repair strategies based on structural outcomes, and identification of process conditions that enrich genomic instability.

These insights enable informed donor selection, process optimization, and risk mitigation strategies that support scalable and consistent manufacturing.

AUTOLOGOUS CELL THERAPIES

Autologous therapies introduce patient-specific biology and often involve complex manufacturing workflows. KROMASURE enables developers to evaluate how editing strategies and culture conditions impact genomic structure within individual patient-derived products, monitor genome integrity during expansion or differentiation, and interpret observed abnormalities in the context of empirically derived benchmarks.

This supports personalized risk assessment while avoiding unnecessary over-testing.

IN VIVO GENE THERAPIES

In vivo approaches require careful evaluation of genomic impact within relevant model systems, including cell lines, organoids, and animal tissues. KROMASURE enables assessment of genome integrity in both dividing and non-dividing cells, characterization of integration-associated structural events, and evaluation of genome integrity risk in contexts where traditional cytogenetic approaches may be limited.

These data provide orthogonal evidence to support safety assessment and regulatory submissions.

Application	Allogenic Cell Therapies	Autologous Cell Therapies	In Vivo Gene Therapies
Manufacturing batch size	Large	Single Patient	Single Patient Treatment
Process tolerance for donor-to-donor variability of genomic stability	Low with proper and comprehensive donor screening	High	High
Risk to Product or Patient genomic integrity	High	Low	High

From Genomic Data to Decisions

KROMASURE enables rapid and decisive decisions throughout discovery, development, and commercialization. By translating single-cell cytogenetic observations into interpretable measures of genomic structure, chromosome integrity, and genome integrity, the platform empowers both technical and strategic decision-making.

During discovery and early development, KROMASURE enables comparison of editing strategies, delivery modalities, and repair pathway modulation based on their impact on genome integrity. These insights support early optimization and go or no-go decisions before processes are locked.

At later stages, genome integrity data inform strategic decisions related to donor selection, process comparability, manufacturing changes, and lifecycle management. By grounding these decisions in quantitative, benchmarked measures, KROMASURE helps align scientific evidence with regulatory expectations and business strategy.

Conclusion

As cell and gene therapies continue to advance, preserving genomic structure and genome integrity is central to long-term success. The KROMASURE platform provides a comprehensive, single-cell cytogenetic framework that integrates whole-genome and targeted assessment, quantitative event burden analysis, and expert interpretation.

By enabling earlier insight into genome integrity risk and supporting informed decisions across development and commercialization, KROMASURE helps cell and gene therapy developers manage complexity, reduce uncertainty, and advance innovative therapies with confidence.

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Genomic Innovation, Cytogenetic Precision

Experience the Next Generation
Structural Genomic Analysis