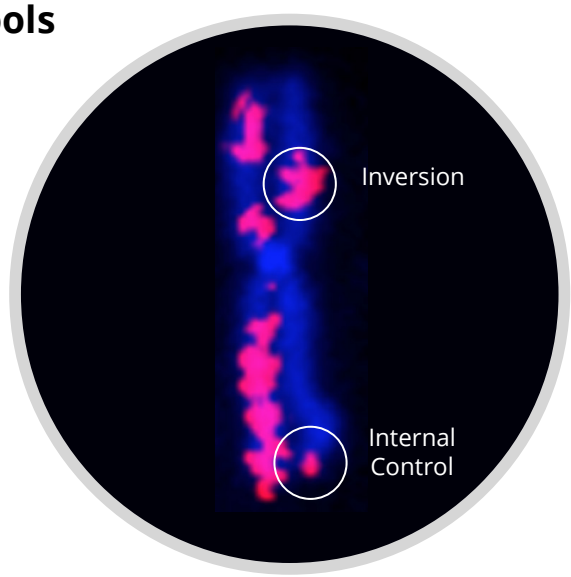
KromaTiD

Directional Genomic Hybridizaiton™ Imaging Products

Transformational Chromosome Imaging Tools

KromaTiD Directional Genomic Hybridization™ (dGH™) imaging technology forms the platform for a wide range of reagents, kits and services that enable the discovery, detection and diagnosis of genetic mutations and diagnostic targets.

The KromaTiD dGH platform is the only technology capable of detecting cryptic inversions - an important class of disease causing mutations. Unlike other chromosome imaging technologies and whole genome approaches, dGH generates gene sequence, location and orientation data in a single rapid assay.



Flexible, High-Performance Chromosome Assays

The foundation of the dGH platform is a library of proprietary short, synthetic, single-stranded DNA probes. Together with unique and optimized assay methods, the dGH platform provides researchers with:

The Broadest Assay Range: In a single assay, KromaTiD products detect the broadest possible spectrum of chromosome rearrangements, including those assayable by standard FISH technologies (e.g. translocations between chromosomes) as well as intra-chromosomal rearrangements such as cryptic inversions. The KromaTiD platform enables orders of magnitude higher-resolution inversion detection than any competing technique.

Chromosome and Chromatid Assay Formats: Using the same probes in different test conditions, KromaTiD assays are capable of targeting entire chromosomes (double-stranded applications like FISH) or individual chromatids (single-stranded applications) in interphase or metaphase cells.

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Visual Orientation Data: When used on metaphase chromosomes, dGH is the only imaging technology capable of providing sequence, location and orientation information in a single assay.

Unique Specificity: Probes are designed to target unique genomic sequences, so KromaTiD assays require no blocking DNA (COT), exhibit no non-specific background, and demonstrate improved hybridization performance.

Quantitative Mutation Size and Location: Because dGH assays are based on a defined library of sequenced and calibrated genomic probes, they can precisely locate and quantitatively size rearrangements.

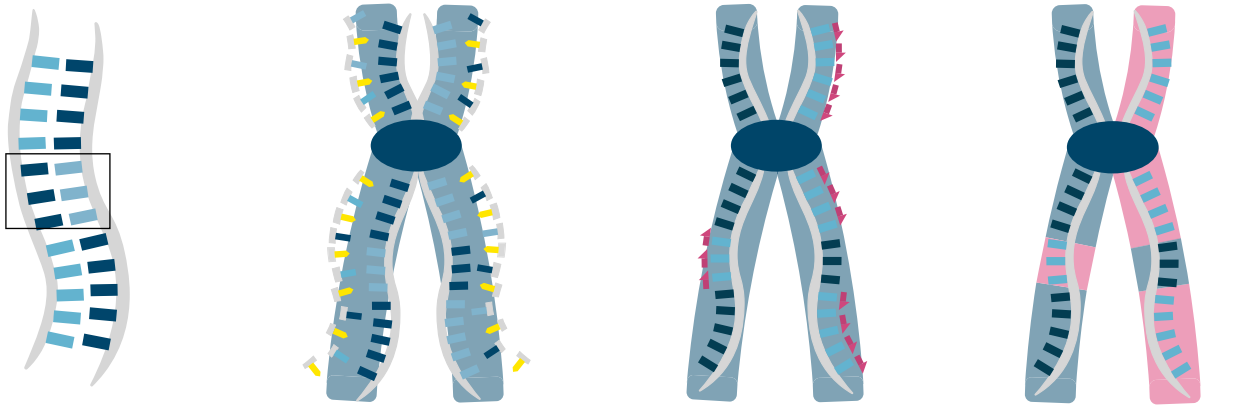
Single Cell Analysis: dGH assays generate imaging data for single cells, not pools of cells, so are ideal for determining mutation heterogeneity within

The Platform

Orientation Detection: For the discovery or detection of inversions, proprietary dGH probes are used with an innovative chromosome preparation in a technique that is capable of determing orientation information from imaging data.[1]

Pre-Replication DNA

Replicated Metaphase Chromosomes in Fixed Cells



Inverted segment in pre-replication interphase DNA

Analog nucleotide incorporation during synthesis enables selective daughter strand degradation

Single-strand-specific unidirectional probe hybridization

Fluorescence microscopy

[1]Ray FA, Zimmerman E, Robinson B, Cornforth MN, Bedford JS, Goodwin EH, Bailey SM (2013) Directional genomic hybridization for chromosomal inversion discovery and detection. Chromosome Res 21(2):165-174

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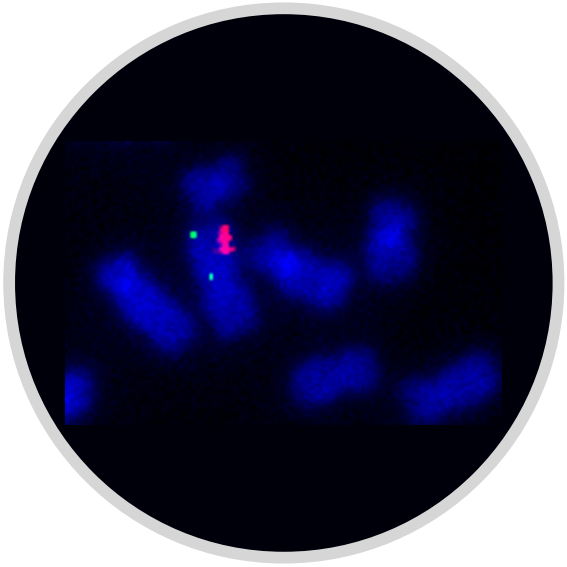
Stock and Custom Assays for the Entire Genome

Pinpoint FISH and Inversion Detection: KromaTiD offers reagents and kits for both inversion detection and Pinpoint FISH applications. Stock chromatid paints, chromosome paints and gene specific assays for inversion screening and discovery, biodosimetry analysis, and known inversion detection (including research-use-only tests for inversion-caused diseases like leukemia and thyroid cancer) are available in 10 and 50 assay kits. New paints and assays are frequently added to the catalog.

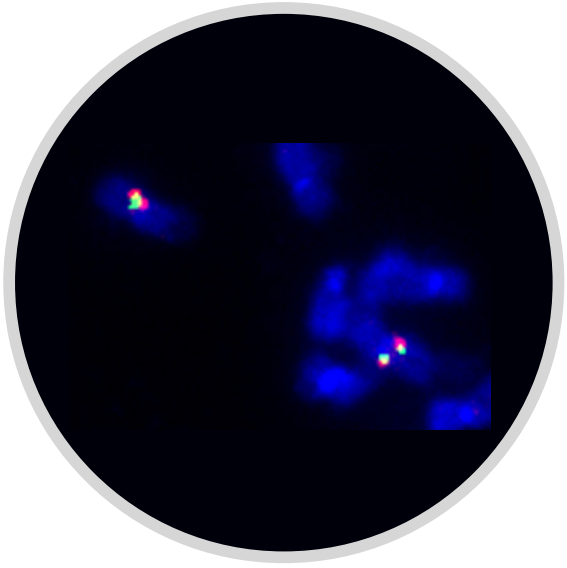
Custom Assays in Weeks: In addition to catalog assays, KromaTiD can rapidly generate custom inversion and Pinpoint FISH assays. Since probes for these custom projects are based on a library of designed, synthetic oligonucleotides (and not vector inserts), tests targeting specific mutations, genes or regions can be designed and produced in a matter of weeks - not months like competitive imaging technologies would require.

Diagnostic Tests: KromaTiD offers research-use-only tests for a number of known inversion-caused diseases including leukemia and thyroid cancer.

Screening and Discovery: dGH assays for the screening and discovery of new cryptic inversions are available for the entire human genome. For newly discovered inversions and other mutations, KromaTiD provides targeted validation assays in both Pinpoint FISH and inversion assay formats.



dGH Detection of Acute Myelogenous Leukemia Inv(3)q21q26)



dGH Detection of Thyroid Cancer Inv(10)(q11.2q21)

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Available dGH Products & Services

dGH Painting Assays for Mutation Discovery on all Chromosomes

- Mutation screening & discovery assays
- Evaluate individual chromosomes
- Analyze specific arms or regions

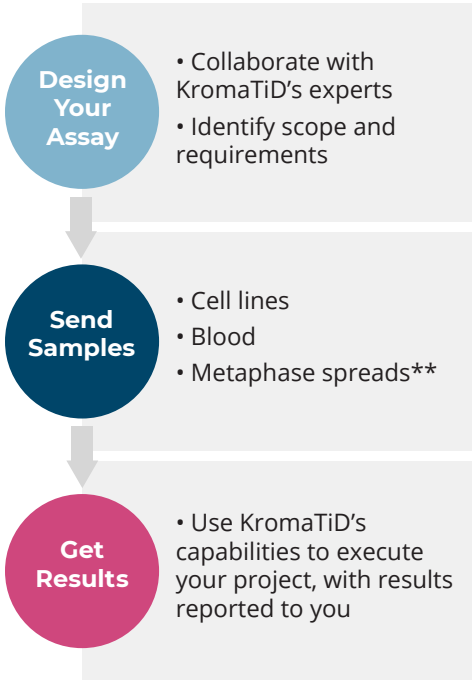
dGH Probe Assays for Specific Mutations

- Gene tracker assays for detecting rearrangements to nearly any gene
- Custom assay development services
- Validation assays for sequencing and arrays

Pinpoint FISH Assays for Specific Mutations

Assay Services for Expert Execution

- Biodosimetry
- Full genome screening
- Custom assay projects



Anonymized or research samples only. Not for diagnostic use.

**Metaphase spreads must be prepped with KromaTiD's protocol to ensure proper assay conditions

dGH Complements the Other Tools in Your Toolbox..

	dGH	G-Banding	FISH	aCGH	Sequencing
Technology	Single strand hybridization	Differntial staining	Double strand hybridization	Double strand hybridization	Whole genome sequencing
Data Dimensions	Sequence, location & orientation	Bands	Sequence & location	Sequence & location	Sequence & location
Single Cell Analysis	Yes	Yes	Yes	No	No
Detectable Mutation Classes	Inter & Intra-Chromosomal	Structural	Structural & inter-chromosomal	Structural & inter-chromosomal	Structural & inter-chromosomal

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dGH is a Uniquely Capable Tool for Inversions..

	dGH	G-Banding	FISH	aCGH	Sequencing
Discover Inversions	High	Low	None	None	Low
Detect Inversions	High	Low	Low	None	Low
Diagnose Inversions	High	Low	Low	None	Low

dGH Provides Broad Mutation Detection in a Single Assay..

	dGH	G-Banding	FISH	aCGH	Sequencing
Balanced Translocation Detection	High	Medium	High	None	Low*
Unbalanced Translocation Detection	High	Medium	High	Medium	Medium
Deletion Duplication	Medium	Low	Low	High	Medium
Duplication Detection	Low	Low	Low	High	Medium
SpeciÞc Sequence Detection	High	None	High	High	High
Inversion Detection	High	Low	Low	None	Low*

*Data analysis is problematic