KREATECH DIAGNOSTICS
CATALOGUE 2013 - 2014

KREATECH
DIAGNOSTICS

FISH4U™

NEW CUSTOM PROBE SERVICE FOR YOU FROM KREATECH

Our flexible custom probe service FISH4U™ gives you access to your probe of choice. We can develop completely new probe designs to your specifications or you can just request an existing DNA probe from our portfolio to be labeled with an alternative color from our range.

Custom made probes

- Leading-edge probe design
- Designed to meet your specifications

REPEAT-FREE™ POSEIDON™ FISH DNA Probes

- A clearer background
- Greater signal intensity

Check out our custom probe service

Contact customer service by mail:
customerservice@kreatech.com
or visit our website:

www.kreatech.com

Disclaimer FISH4U:

The Customer acknowledges that no licenses or other rights are provided to the Customer under any patents, patent applications, trade secrets or other proprietary rights of Kreatech, except the right to conduct research.

Kreatech retains ownership of the Product and Kreatech is free to commercialize the Product to any third party except if customer has rights or desires to receive rights to such probe as designed, developed and produced by Kreatech.

If the Customer desires to use the Product for commercial purposes and/or acquire exclusive rights in the Product, the Customer agrees, in advance of such use, to negotiate in good faith with Kreatech to establish the terms of such an agreement.

WELCOME TO THE KREATECH DIAGNOSTICS 2013-2014 CATALOGUE

As a leader in molecular diagnostics we can offer you the broadest portfolio of Fluorescent In Situ Hybridization (FISH) probes available. Our REPEAT-FREE™ POSEIDON™ FISH probes and the unique ULS™-labeling technology are used for diagnostic- and (clinical) research applications worldwide.

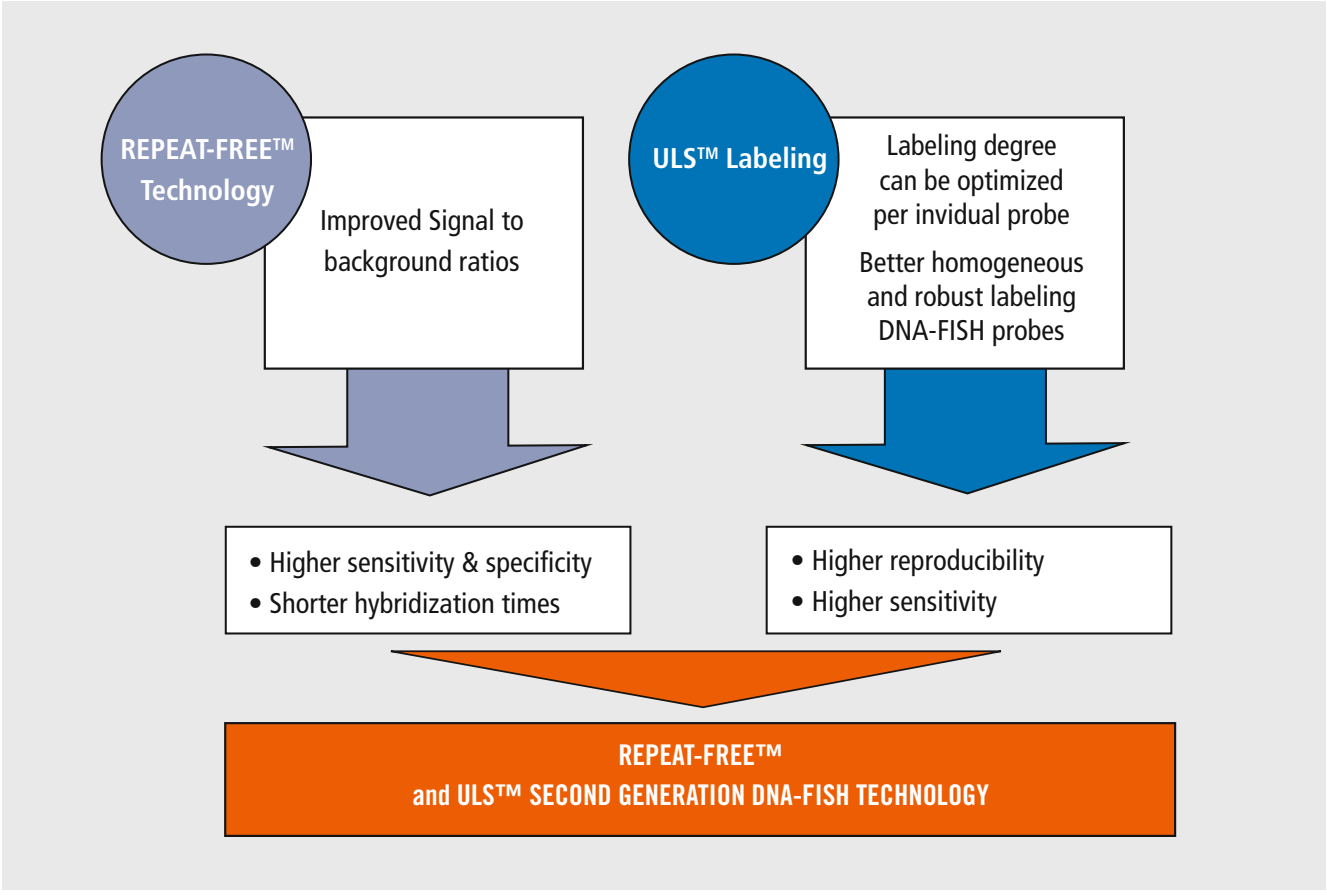
We continuously strive to increase our level of customer- and technical services, as we are committed to delivering high-performance innovative products. Building on collaborations with leading scientists and global partners we continue to invest in advancing diagnostics and science by continuing to expand the portfolio of our REPEAT-FREE™ POSEIDON™ FISH probes.

To meet the ever-growing demand of high-quality DNA FISH probes throughout the scientific and diagnostic communities, we have made our expertise in developing REPEAT-FREE™ POSEIDON™ FISH probes available through our custom design program – FISH4U™. This custom probe service allows you to get access to DNA FISH probes that are tailored to your application.

Check our website at www.kreatech.com on a regular basis for up to date information on our products. On our website you can also find the KREATECH chromosome finder: an easy-to-use tool that will guide you through our range of FISH-probes.

We look forward to serving you in the coming years. Your trusted partner in molecular diagnostics and microarray labeling applications.

KREATECH Diagnostics



This Catalogue is not intended for the Unites States of America. If you are interested in more information for the North American Region please scan the QR Code with your mobile phone which can be found on the right side: or go to www.KREATECH.com

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REPEAT-FREE POSEIDON FISH DNA PROBES

Kreatech Diagnostics offers the next generation REPEAT-FREE™ POSEIDON™ DNA probes developed with the use of the REPEAT-FREE (RF) technology.

This technology is based on a proprietary subtractive hybridization specifically removing all repetitive elements which are dispersed throughout the human genome. Eliminating these repeat sequences leads to a more specific binding kinetics and makes the need to use C_0t1 DNA for pre-annealing obsolete. In addition, our DNA probes are labeled with Kreatech's proprietary ULS™ linkage system leading to a very homogenous and consistent labeling of fluorescent dyes.

This results in FISH probes that are brighter and give a clearer background.
The signal to noise ratio of RF POSEIDON FISH probes in comparison to standard probes today is 1.5 to 3 times greater.

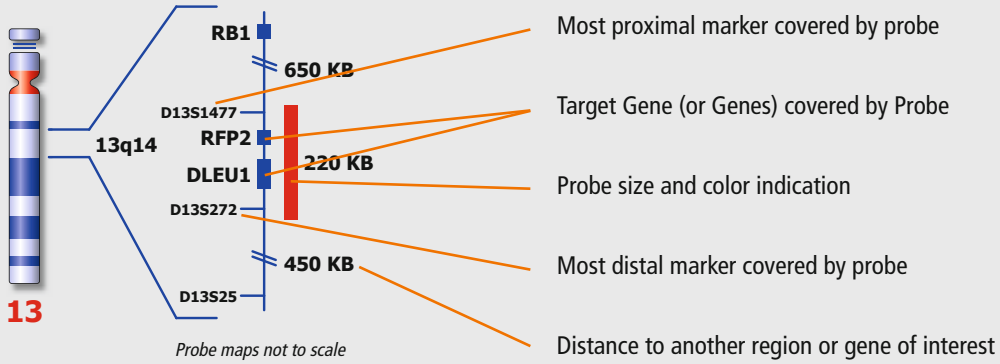
Our recommended Pretreatment Kits with Ready-to-Use reagents makes the pretreatment of different tissue and cytological samples easier and guarantees optimal results in combination with the RF POSEIDON FISH probes.

Traditional FISH is very time consuming with standard hybridizations being on average 16 hours in duration. With the use of RF POSEIDON FISH probes, hybridization times may be cut 75% to 4 hours.

This hybridization flexibility coupled with optimal pretreatment and the probes being available in a Ready-to-Use format eliminates time consuming steps and optimizes workflow.

The POSEIDON™ Probe Maps

All locus specific probes are provided with a map showing the genome region and/or genes the probe cover. The STS markers indicating the most proximal and distal end covered by the probe are added as well. Those markers can be used to describe in situ hybridization results in accordance with the International System for Human Cytogenetic Nomenclature (ISCN, 2013). For more information see e.g. Genome Browser at genome.ucsc.edu or Ensemble at www.ensembl.org



Fluorophores and filter recommendations

Please check out the website www.kreatech.com for recommended filters covering the excitation and emission wavelenghts as specified below.

When ordering a filter from a supplier please make sure to either have a cube or slider available for your specific brand and type of microscope.

Single Filters

Fluorophore	Color	Ex/Em	Recommended Filter	Excitation Filter	Dichromatic Mirror	Emission Filter
DAPI	DAPI		DAPI / UV	360/20	400 LP	425 LP
Platinum*Bright*™405	Dark Blue	410/455	Blue	405/10	425 LP	460/50
Platinum*Bright*415	Blue	429/470	Aqua	436/20	455 LP	480/30
Platinum*Bright*495	Green	495/517	FITC / Green	480/30	505 LP	535/40
Platinum*Bright*505	Green	500/528	FITC / Green	480/30	505 LP	535/40
Platinum*Bright*530	Gold	531/561	Gold	520/18	545 LP	565/20
Platinum*Bright*547	Light Red	547/565	Cy3	535/50	565 LP	610/75
Platinum*Bright*550	Red	550/580	TRITC	540/25	565 LP	605/55
Platinum*Bright*570	Red	570/591	Texas Red	560/40	595 LP	645/75
Platinum*Bright*590	Dark Red	587/612	Texas Red	560/40	595 LP	645/75
Platinum*Bright*647	Far Red	647/665	Cy5 / Far red	620/60	660 LP	700/75

Dual/Triple Filters

Fluorophore	Color	Recommended Filter	Excitation Filter	Dichromatic Mirror	Emission Filter
Platinum*Bright*495/550	Green/Red	Dual FITC/Cy3	485/10 563/12	500-550 580 LP	521/20 595 LP
Platinum*Bright* 415/495/550	Blue/Green/Red	DAPI/FITC/Cy3	430/12 490/12 562/12	446-478 503-548 579 LP	463/10 523/15 585 LP
DAPI / Platinum*Bright* 495/550	DAPI/Green/Red	DAPI/FITC/ TRITC or Cy3	396/8 482/8 554/14	440-472 498-540 573 LP	450/10 516/20 604/22

CATALOGUE 2013-2014 – **NEW PRODUCTS**

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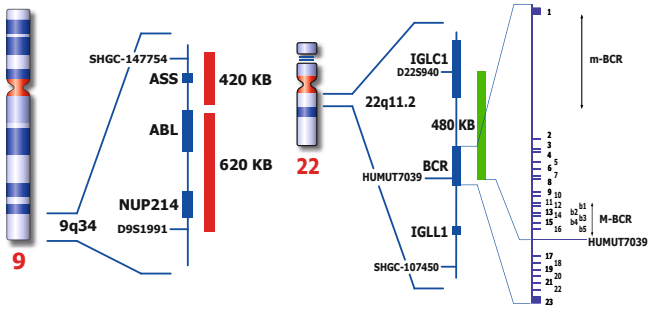
* All Microdeletion DNA Probes are available in a 5 or a 10 test format.

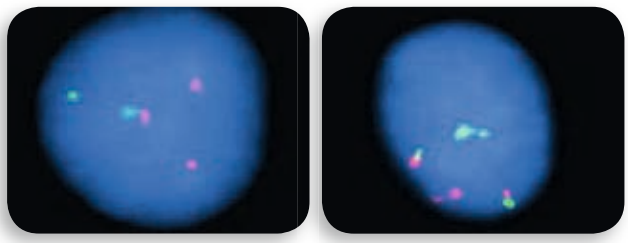
CML

ON Mm-BCR/ABL t(9;22), DC, S-Fusion, ES

Chronic Myeloid Leukemia (CML) is characterized by the formation of the BCR/ABL fusion gene as a result of the reciprocal translocation t(9;22)(q34;q11). The BCR/ABL fusion gene is found on the derivative chromosome 22, called the Philadelphia (Ph) chromosome. The same translocation is also observed in Acute Lymphocytic Leukemia (ALL) and in Acute Myeloid Leukemia (AML). This chimeric BCR/ABL gene encodes a constitutively activated protein tyrosine kinase with profound effects on cell cycle, adhesion, and apoptosis. Understanding this process has led to the development of the drug imatinib mesylate (Gleevec™).
Breakpoints in the BCR gene region can occur in different regions, predominately in a major breakpoint cluster region (M-BCR) but can also occur in a minor breakpoint cluster region (m-BCR) or micro breakpoint cluster region (µ-BCR). Further research indicates that CML patients with different BCR-ABL transcripts respond differently to treatment with Gleevec.

Cat# KBI-10013 Mm-BCR/ABL t(9;22), DC, S-Fusion, ES





Mm-BCR/ABL probes hybridized to patient material showing t(9;22) with M-BCR (1F1r1R1G).

Mm-BCR/ABL probes hybridized to patient material showing t(9;22) with m-BCR (2F1R1G).

Literature:

Dewald et al., 1998, Blood 91; 3357-3365.
Huntly et al., 2003, Blood 102; 1160-1168.
Sharma et al., 2010, Ann Hematol, 89, 241-7.
Tkachuk et al., 1990, Science 250, 559-56.
Kolomietz et al., 2001. Blood 97; 3581-3588.

Ordering information	*Gene Region*	*Tests*	*Cat#*
ON Mm-BCR/ABL t(9;22), DC, S-Fusion, ES	green/red	10	KBI-10013

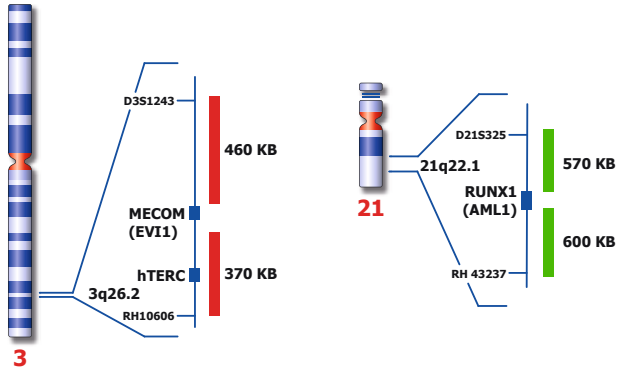
AML

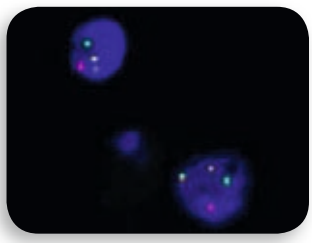
ON MECOM / RUNX1 t(3;21) Fusion

The MECOM (EVI1, 3q26) / RUNX1 (AML1, 21q22) translocation, t(3;21), is consistently found in blastic crisis of chronic myelogenous leukemia (CML) and myelodysplastic syndrome-derived leukemias. The translocation produces MECOM / RUNX1 chimeric transcription factor and is thought to play important roles in acute leukemic transformation of hemopoietic stem cells.

The MECOM/RUNX1 t(3;21)(q26;q22) specific DNA Probe is optimized to detect the reciprocal translocation t(3;21) in a dual-color, dual-fusion assay on metaphase/interphase spreads, blood smears and bone marrow cells.

Cat# KBI-10310 MECOM / RUNX1 t(3;21) Fusion





MECOM / RUNX1 Fusion probe hybridized to patient material showing t(3;21) (2F1R1G).
Images kindly provided by Dr. Mohr, Dresden.

Ordering information	*Gene Region*	*Tests*	*Cat#*
ON MECOM / RUNX1 t(3;21) Fusion	red/green	10	KBI-10310

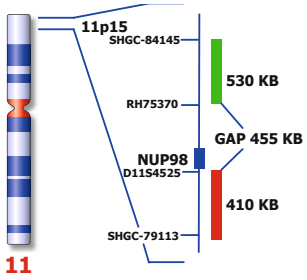
ALL

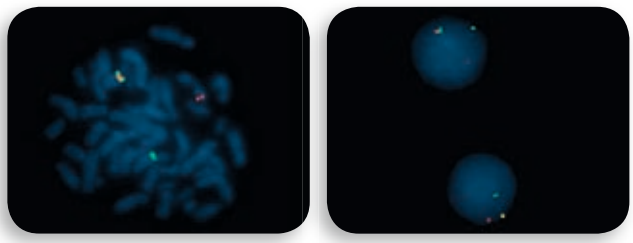
NUP98 (11p15) Break

Nucleoporin 98kDa gene (NUP98) rearrangements have been identified in a wide range of hematologic malignancies, including acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), chronic myeloid leukemia in blast crisis (CML-bc), myelodysplastic syndrome (MDS) and bilineage/ biphenotypic leukemia. The NUP98 gene is highly promiscuous with regard to its recombination spectrum, as at least 28 different partner genes have been identified for NUP98 rearrangements, all forming in-frame fusion genes. Patients with NUP98 gene rearrangements have an aggressive clinical course and the outcome of treatment is disappointing.

The NUP98 (11p15) Break Probe is optimized to detect translocations involving the NUP98 gene region at 11p15 in a dual-color assay on metaphase/interphase spreads, blood smears and bone marrow cells.

Cat# KBI-10311 NUP98 (11p15) Break





NUP98 (11p15) Break Probe hybridized to AML patient sample showing a rearrangement of 11p15 involving the NUP98 gene (1F1R1G).

Images kindly provided by Prof. Manuel R. Teixeira, Porto.

Literature:

Gough et al, 2011, Blood 118; 62 47-6257.
Nebral et al, 2005, Haematologica 90; 74 6-752.
Romana et al, 2006, Leukemia 20; 696-70 6.

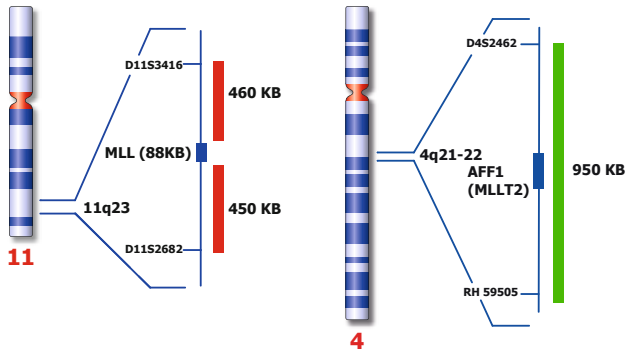
Ordering information	*Gene Region*	*Tests*	*Cat#*
NUP98 (11p15) Break	red/green	10	KBI-10311

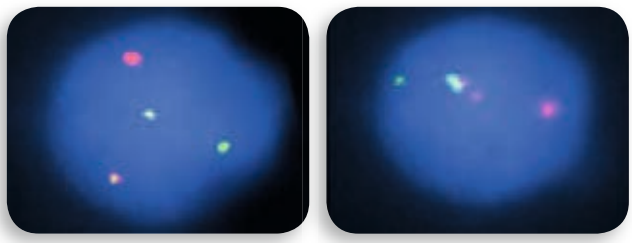
ON MLL/AFF1 t(4;11) Fusion

The t(4;11) MLL/AFF1 is the most frequently (approximately 66% according to Meyer et al.) observed translocation involving the MLL gene resulting in Acute Lymphoblastic Leukemia (ALL). The MLL/AFF1 translocation results in the generation of fusion proteins MLL/AFF1 and AFF1/MLL; both seem to have leukemogenic properties. Furthermore, EVI1 (3q26) is one of the targets of the MLL oncoproteins, which increased expression correlates with unfavorable prognosis in Acute Myeloid Leukemia. Patients with ALL and the MLL/AFF1 translocation are associated with a high risk of treatment failure.

The MLL/AFF1 t(4;11) Fusion Probe is optimized to detect translocations involving the MLL and AFF1 gene regions at 4q21-22 and 11q23 in a dual-color, fusion assay on metaphase/ interphase spreads, blood smears and bone marrow cells.

Cat# KBI-10404 MLL/AFF1 t(4;11) Fusion





MLL/AFF1 t(4;11) Fusion Probe. Standard t(4;11) 2 Fusion, 1 Red, 1 Green (2F1R1G).

MLL/AFF1 t(4;11) Fusion Probe. ins(4;11) 1F2R1G.

Literature

Harrison CJ et al, 2010, Br J Haem, 151; 132-142.
Arai S et al, 2011, Blood, 117; 6304 - 6314.
Meyer C et al, 2009, Leukemia, 23; 1490-1499.

Ordering information	*Gene Region*	*Tests*	*Cat#*
ON MLL/AFF1 t(4;11) Fusion	red/green	10	KBI-10404

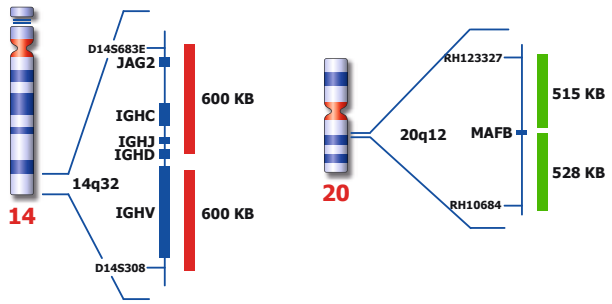
MM

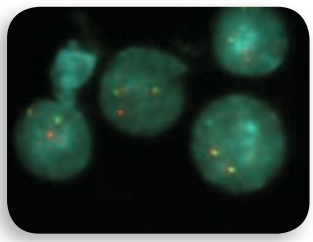
ON MAFB/IGH@ t(14;20) Fusion

The immunoglobulin heavy chain (IGH@) gene at 14q32 is an important cause of genetic deregulation in multiple myeloma (MM). Among the known fusion partners for the IGH gene, reciprocal translocation with the MAFB gene at 20q12 is relatively rare in MM (~2% occurrence). However, the MAFB/IGH@ t(14;20) translocation is associated with poor prognosis in multiple myeloma patients.

The MAFB/IGH@ t(14;20) Fusion Probe is optimized to detect the reciprocal translocation t(14;20) in a dual-color, dual-fusion assay on metaphase/interphase spreads and bone marrow cells.

Cat# KBI-10510 MAFB/IGH@ t(14;20) Fusion





The MAFB/IGH@ t(14;20) Fusion Probe hybridized to patient material showing a complex pattern with a t(14;20) translocation.
Images kindly provided by Erasmus Medical Center, Rotterdam..

Literature:

Boersma-Vreugdenhil GR et al, 2004, Br J Haematol, 126, 355-363.
Bergsagel PL et al, 2005, JCO, 23, 6333-6338.

Ordering information	*Gene Region*	*Tests*	*Cat#*
ON MAFB/IGH@ t(14;20) Fusion	red/green	10	KBI-10510

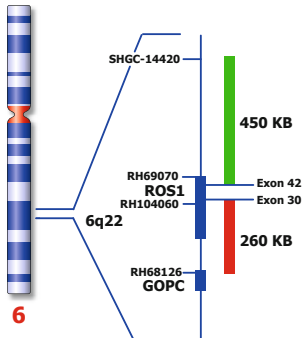
Lung Cancer

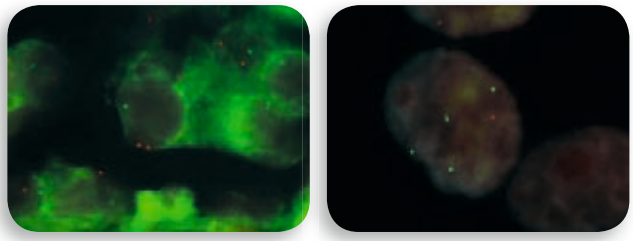
ON ROS1 (6q22) Break

Translocations involving the ROS1 (repressor of silencing 1) gene at chromosome 6q22 can increase expression of the gene by fusion with SLC34A2 (4p15), but also with other fusion partners. Elevated expression is observed in non-small cell lung cancer (NSCLC), where the success of tyrosine kinase-based therapeutics is based on inhibiting the activity of these fusion genes. The fusion of ROS1 to the GOPC (FIG; 6q22) gene, by deletion of a 240 kb DNA fragment, also results in activation of a fusion gene.

The ROS1 (6q22) Break Probe is optimized to detect translocations involving the ROS1 gene region at the 6q22 locus, as well as the 240 kb deletion forming the ROS1-GOPC fusion gene, in a dual-color assay on formalin- fixed paraffin-embedded tissue samples.

Cat# KBI-10752 ROS1 (6q22) Break





Hybridization of ROS1 (6q22) Break Probe (KBI-10752) to a tissue section harboring a ROS1 rearrangement.

Hybridization of ROS1 (6q22) Break Probe (KBI-10752) to a cell line harboring a GOPC-ROS1 rearrangement (deletion of red signal).

Literature:

Charest et al., Genes Chromosomes Cancer, 2003, 37: 58-71.
Rikova et al., Cell, 2007, 131: 1190-120.
Rimkunas et al., Clin. Can. Res., 2012, 18: 4449-4457.
Takeuchi et al., Nat. Med., 2012, 18: 378-381.
Gu et al., PLoS, 2011, 6: e15640.

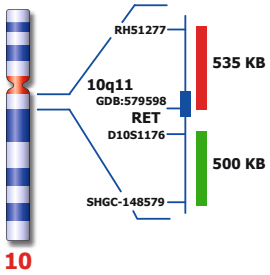
Ordering information	*Gene Region*	*Tests*	*Cat#*
ON ROS1 (6q22) Break	green/red	10	KBI-10752

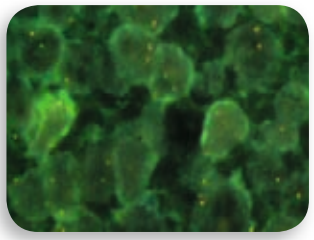
ON RET (10q11) Break

Pericentric inversion of chromosome 10 involving the RET (ret proto-oncogene) gene at chromosome 10q11 is known to increase expression of the RET gene by fusion with KIF5B (10p11). Translocations with other fusion partners have also been described. Elevated expression of RET is observed in non-small cell lung cancer (NSCLC), in which the function of tyrosine kinase-based therapeutics is based upon the inhibition of such fusion proteins. Translocations involving RET have also been described in thyroid carcinomas.

The RET (10q11) Break Probe is optimized to detect translocations involving the RET gene region at the 10q11 locus..

Cat# KBI-10753 RET (10q11) Break





Hybridization of RET (10q11) Break Probe (KBI-10753) to a tissue section.

Literature:

Chen et al., Cancer Genet Cytogenet, 2007, 178: 128-134.
Kohno et al. , Nat Med, 2012, 18: 375-377.
Takeuchi et al., Nat Med, 2012, 18: 378-381.

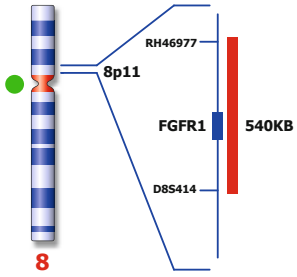
Ordering information	*Gene Region*	*Tests*	*Cat#*
ON RET (10q11) Break	red/green	10	KBI-10753

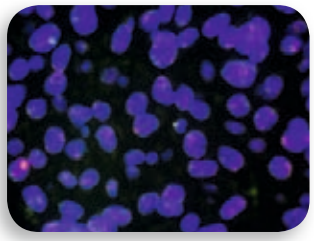
FGFR1 (8p11) / SE 8 (D8Z1)

Amplification of the fibroblast growth factor receptor type 1 gene (FGFR1) has been observed in numerous cancer types including lung cancer (especially squamous cell carcinoma) and breast cancer. With the development of new therapeutic strategies, FGFR1 amplification could act as a valuable biomarker for R&D and provide an attractive tool for clinical stratification[2].

The FGFR1 (8p11) / SE8 Amplification probe is optimized to detect amplification involving the FGFR1 gene region at 8p11 in a dual-color assay on paraffin embedded tissue sections.

Cat# KBI-12754 / KBI-14754 FGFR1 (8p11) / SE 8 (D8Z1)





FGFR1 gene locus amplification in FFPE NSCLC tissue.

Literature:

Weiss et al., 2010, Sci. Transl. Med. 2(62): 62ra93.
Brooks et al., 2012, Clin. Cancer Res. 18(7): 1855-62.

Ordering information	*Gene Region*	*Tests*	*Cat#*
FGFR1 (8p11) / SE 8 (D8Z1)	red/green	20	KBI-12754
FGFR1 (8p11) / SE 8 (D8Z1)	red/green	50	KBI-14754

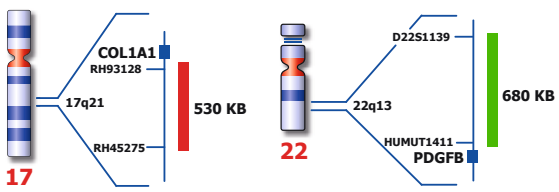
Sarcoma

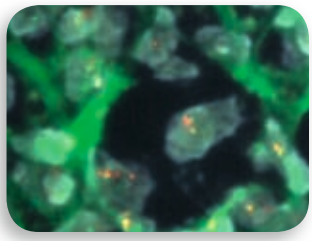
ON COL1A1/PDGFB t(17;22) DC, S-Fusion

The diagnosis of primary soft tissue and bone tumors is often challenging as they are relatively rare. The misdiagnosis between dermatofibroma (DF) and dermatofibrosarcoma protuberans (DFSP) or giant cell fibroblastoma (GCF) might result in improper primary management. DFSP and GCF have in most cases diagnosed today a translocation involving the COL1A1 (collagen, type I, alpha 1) gene at 17q21 and the PDGFB (platelet-derived growth factor beta polypeptide) gene at 22q13. Also, a supernumerary ring chromosome derived from the translocation r(17;22) can be present.

The COL1A1/PDGFB t(17;22) Dual-Color Single-Fusion Probe is optimized to detect the t(17;22)(q21;q13) involving the COL1A1 (17q21) and PDGFB (22q13) gene regions in dual-color, single-fusion assay on paraffin embedded tissue sections.

Cat# KBI-10742 COL1A1/PDGFB t(17;22) DC, S-Fusion





Interphase FISH result of ON COL1A1/PDGFB Fusion probe hybridized to dermatofibrosarcoma protuberans tumor tissue. Co-localisation and amplification of the fusion gene is well visible.

Literature:

Maire et al, 2007, Arch Dermatol, 143; 203-210.
Labropoulos et al, 2007, Biologics, 1; 347-353.
Patel et al, 2008, Hum Path, 39; 184-193.
Sandberg, 2003, Cancer Genet Cytogenet, 140; 1-12.

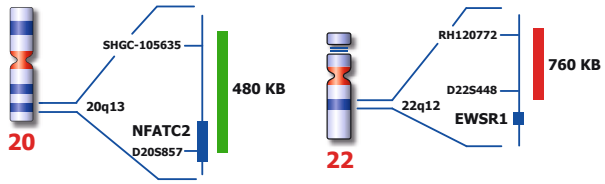
Ordering information	*Gene Region*	*Tests*	*Cat#*
ON COL1A1/PDGFB t(17;22) DC, S-Fusion	red/green	10	KBI-10742

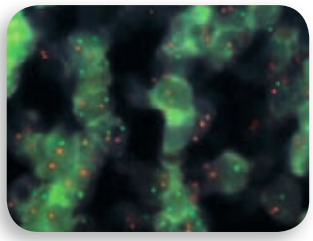
ON EWSR1/NFATC2 t(20;22) DC, S-Fusion

Ewing's sarcoma is the second most frequent primary bone cancer. In most cases a translocation involving the EWSR1 gene at 22q12 and the FLI1 gene at 11q24 is observed. Several other translocation partners of the ETS gene family can also be involved. The first non-ETS family translocation partner described is the NFATC2 gene (nuclear factor of activated T-cells, cyto-plasmic, calcineurin-dependent 2) at 20q13.

The EWSR1/NFATC2 single fusion probe is best used to analyze the specific trans-locations of the EWSR1 and NFATC2 gene on formalin fixed paraffin embedded tissue for routine clinical diagnosis.

Cat# KBI-10751 EWSR1/NFATC2 t(20;22) DC, S-Fusion





Interphase FISH result of the EWSR1/NFATC2 t(20;22) DC, S-Fusion probe.

Literature:

Szuhai et al, 2009, Clin Cancer Res, 15; 2259-2268.
Zucman-Rossi et al, 1998, PNAS, 95; 11786-11791.
Bernstein et al, 2006, Oncologist, 11; 503-519.

Ordering information	*Gene Region*	*Tests*	*Cat#*
ON EWSR1/NFATC2 t(20;22) DC, S-Fusion	red/green	10	KBI-10751

Lymphoma (tissue)

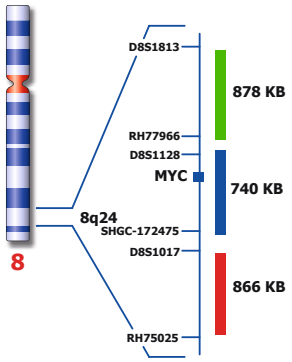
ON MYC (8q24) Break, TC (tissue)

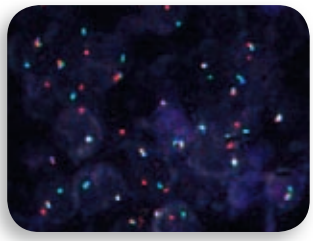
Rearrangements of the proto oncogene C-myc (or MYC) have been consistently found in tumor cells of patients suffering from Burkitt's lymphoma. In cases with the common t(8;14) chromosomal translocation, the c-myc gene is translocated to chromosome 14 and rearranged with the immunoglobulin heavy chain genes; the breakpoint occurs 5' to the c-myc gene and may disrupt the gene itself separating part of the first untranslated exon from the remaining two coding exons. In Burkitt's lymphoma showing the variant t(2;8) or t(8;22) translocations, the genes coding for the k and l immunoglobulin light chain are translocated to chromosome 8.

The MYC (8q24) break-apart probe is optimized to detect rearrangements involving the 8q24 locus in a triple-color, split assay on formalin fixed paraffin embedded tissue.

In addition Kreatech has developed a probe for the specific use on cell material (KBI-10611).

Cat# KBI-10749 MYC (8q24) Break, TC (tissue)





MYC (8q24) Break, TC (tissue) probe hybridized to patient material showing a 8q24 distal break (1GB1R1GBR).
Image kindly provided by N. Van Acker, HistoGeneX, Antwerp.

Literature:

Fabris et al, 2003, Genes Chromosomes Cancer 37; 261-269.
Hummel et al, 2006, N Engl J Med 354; 2419-30.

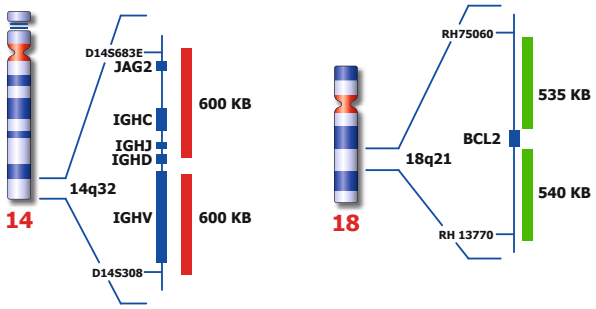
Ordering information	*Gene Region*	*Tests*	*Cat#*
ON MYC (8q24) Break, TC (tissue)	red/green/blue	10	KBI-10749

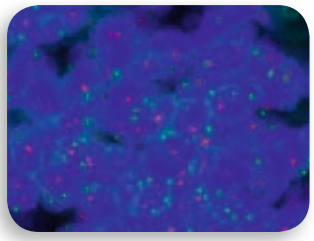
ON BCL2/IGH@ t(14;18) Fusion (tissue)

Follicular lymphoma is a mature B-Cell lymphoma, characterized by the presence of the t(14;18) translocation that juxtaposes the BCL2 locus on chromosome 18q21 to the immunoglobulin H (IGH) locus on chromosome 14q32, resulting in the overexpression of the antiapoptotic protein BCL2.

The BCL2/IGH@ t(14;18) Fusion Probe is optimized to detect the reciprocal translocation t(14;18) in a dual-color, dual-fusion assay on formalin fixed paraffin embedded tissue samples. In addition KREATECH has developed a probe for the specific use on cell material (KBI-10606).

Cat# KBI-10755 BCL2/IGH@ t(14;18) Fusion (tissue)





BCL2/IGH@ t(14;20) Fusion Probe hybridized to paraffin embedded lymph node material.
Image kindly provided by Philippa May, Imperial College, Hammersmith Hospital, London.

Literature:
Taniwaki M et al, 1995, Blood, 86; 1481-1486.
Poetsch M et al, 1996, J Clin Oncol, 14; 963-969.

Ordering information	*Gene Region*	*Tests*	*Cat#*
ON BCL2/IGH@ t(14;18) Fusion (tissue)	red/green	10	KBI-10755

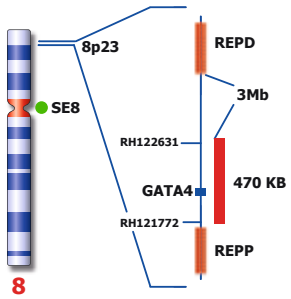
MICRODELETION

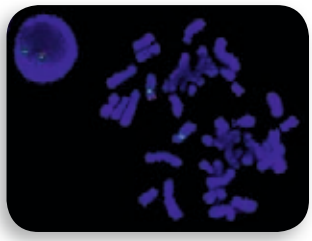
MD GATA4 (8p23) / SE 8

The deletion of GATA4 (8p23) is found in patients with congenital heart disease. Besides the deletion of the region, duplications are found of the region flanked by low copy repeats 8p-OR-REPD (distal) and –REPP (proximal). These recurrent deletions are associated with a spectrum of anomalies, including congenital diaphragmatic hernia, developmental delay and neuropsychiatric findings. GATA4 is expressed in adult heart, epithelium and gonads. During fetal development, GATA4 is expressed in yolk sac endoderm and cells involved in heart formation.

The MD GATA4 (8p23) / SE 8 probe is optimized to detect deletions of the GATA4 gene region at 8p23 in a dual color assay on metaphase/interphase spreads, blood smears and bone marrow cells. The Chromosome 8 Satellite Enumeration (SE) probe is included to facilitate chromosome identification.

Cat# KBI-40118 GATA4 (8p23) / SE 8





GATA4 (8p23) / SE 8 Probe hybridized to patient material showing a deletion of the GATA4 (8p23) region (1R2G).
Image kindly provided by Dr. Marie-France Portnoï, Service de génétique et embryologie médicales Hôpital Armand-Trousseau, Paris.

Literature:
Bhatia et al, 1999, Prenat Diagn, 19, 863-867.
Giorda et al, 2007, Hum Mut, 28, 459-468.
Wat et al, 2009, Am J Med Genet Part A, 149A, 1661-1677.

Ordering information	*Gene Region*	*Tests*	*Cat#*
MD GATA4 (8p23) / SE 8	red/green	5	KBI-45118
MD GATA4 (8p23) / SE 8	red/green	10	KBI-40118

ONCOLOGY - HEMATOLOGY DNA PROBES

From the 25,000 genes in the human genome, approximately 350 genes have been causally linked to the development of cancer. Variant or aberrant function of these so-called cancer genes may result from changes in genome copy number (through amplification, deletion, chromosome loss, or duplication), changes in gene and chromosome structure (through chromosomal translocation, inversion, or other rearrangements that lead to chimeric transcripts or deregulated gene expression) and point mutations (including base substitutions, deletions, or insertions in coding regions and splice sites).

The vast majority (90%) of cancer genes are mutated or altered through chromosomal aberrations in somatic tissue, about 10% are altered in the germ line, thereby transmitting heritable cancer susceptibility through successive generations. In addition to high resolution chromosome banding and advanced chromosomal imaging technologies, chromosome aberrations in cancer cells can be analyzed with an increasing number of large-scale, comprehensive genomic and molecular genetic technologies – including Fluorescence *In Situ* Hybridization (FISH).

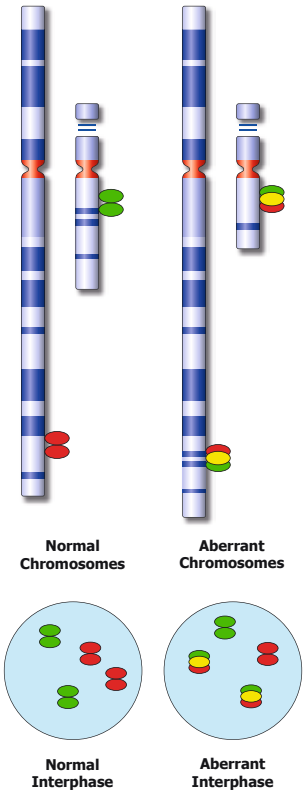
The REPEAT-FREE™ POSEIDON™ Hematology DNA Probes are direct labeled, Ready-to-Use in hybridization buffer and available in a 10 test kit. The hematology probes are designed for use on interphase, metaphase chromosomes from cultured peripheral blood cells or cultured bone marrow samples. Most of the lymphoma probes are also optimized for use on FFPE tissue material and can be found at the product section solid tumor probes.

Table of Contents

Translocation, Dual-Fusion Assay

Dual-fusion, dual-color FISH assays for translocation utilize large probes that span 2 breakpoints or flanking regions on the different chromosomes. Dual-fusion, dual-color FISH is optimal for detection of low levels of nuclei possessing a simple balanced translocation, as it greatly reduces the number of normal background nuclei with an abnormal signal pattern.

Translocation, Dual-Fusion Assay



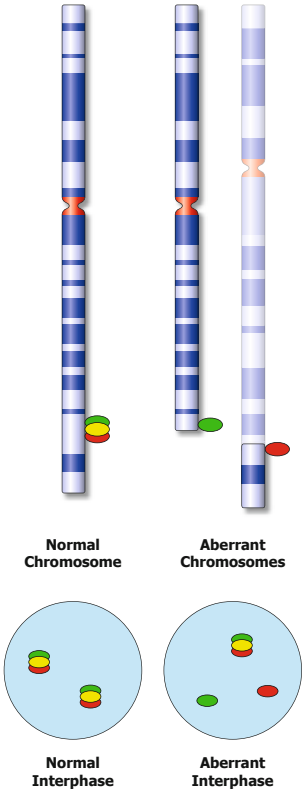
Expected signal pattern:

In normal intact cells, two separate red and two separate green individual signals will be visible, whereas a reciprocal translocation will generate two fused red/green signals (often appearing as single yellow signals), accompanied by one red and one green signal (representing the normal chromosomes).

Translocation, Break-Apart or Split Assay

FISH using dual-color, break-apart probes is very useful in the evaluation of genes known to have multiple translocation partners; the differently colored probes hybridize to targets on opposite sides of the breakpoint of the affected gene.

Translocation, Break or Split Assay



Expected signal pattern:

In normal cells two sets of red/green-fused signals (representing the two alleles) will be visible. In an abnormal diploid cell, in which one allele has been split by a translocation, a separated red and green signal will be visible in addition to the normal fused signal.

Chronic Myeloproliferative Disorders (CMPD)

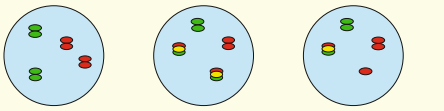
Chromosomal translocations in chronic myeloproliferative diseases (CMPD) almost invariably correlated with expression of constitutively activated fusion tyrosine kinases. The hallmark of these diseases is CML, where the BCR/ABL activated tyrosine kinase results from the balanced reciprocal Philadelphia chromosome translocation t(9;22).

Chronic Myelogenous Leukemia (CML) - BCR/ABL t(9;22)

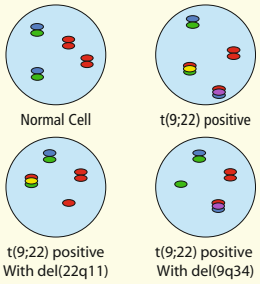
CML is a malignant chronic myeloproliferative disorder (MPD) of the hematopoietic stem cell. All CML have a t(9;22) resulting from fusion of the 3' ABL region at 9q34 with the 5' BCR region at 22q11. This chimeric BCR/ABL gene encodes a constitutively activated protein tyrosine kinase with profound effects on cell cycle, adhesion, and apoptosis. Understanding this process has led to the development of the drug imatinib mesylate (Gleevec™), the first in a new class of genetically targeted agents, this is a major advance in cancer treatment. Several different approaches are used to analyze the BCR/ABL t(9;22)(q34;q11) by FISH each providing different details about this translocation.

Interpretation guidelines for POSEIDON™ BCR/ABL Probes

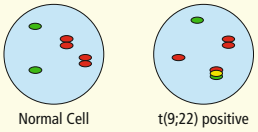
BCR/ABL t(9;22) Dual-color, Dual-Fusion Probe



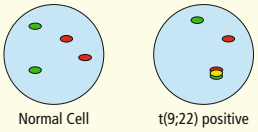
BCR/ABL t(9;22) Triple-color, Dual-Fusion Probe



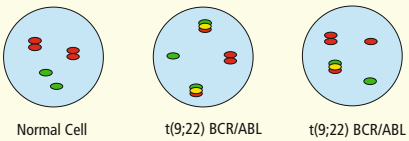
BCR/ABL t(9;22) Dual-color, Single-Fusion Extra Signal Probe



BCR/ABL t(9;22) Dual-color, Single-Fusion Probe



Mm-BCR/ABL t(9;22) Dual-Color, Single-Fusion, Extra Signal

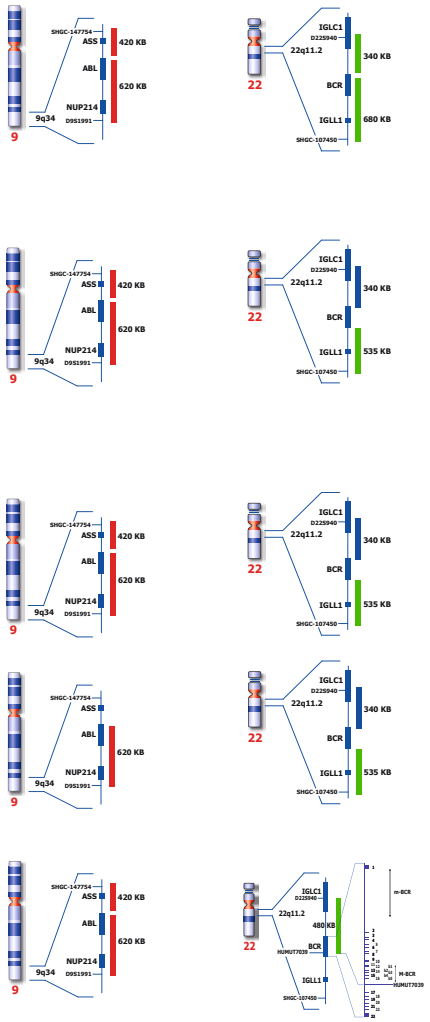


BCR/ABL Product Family

The Philadelphia chromosome is an abnormally short chromosome 22 that is one of the two chromosomes involved in a translocation with chromosome 9. This translocation t(9;22)(q34;q11) takes place in a single bone marrow cell and, through the process of clonal expansion, gives rise to the leukemia.

ABL and BCR are genes on chromosomes 9 and 22, respectively. The ABL gene encodes a tyrosine kinase enzyme whose activity is tightly controlled. In the formation of the Ph translocation, two fusion genes are generated: BCR-ABL on the Ph chromosome and ABL-BCR on the chromosome 9 participating in the translocation. The BCR-ABL gene encodes a protein with deregulated tyrosine kinase activity.

The presence of this protein in the CML cells is strong evidence of its pathogenetic role. The efficacy in CML of a drug that inhibits the BCR-ABL tyrosine kinase has provided the final proof that the BCR-ABL oncoprotein is the unique cause of CML. The POSEIDON™ portfolio contains now 4 different probes for BCR/ABL to suit all needs for the detection of t(9;22) by FISH:

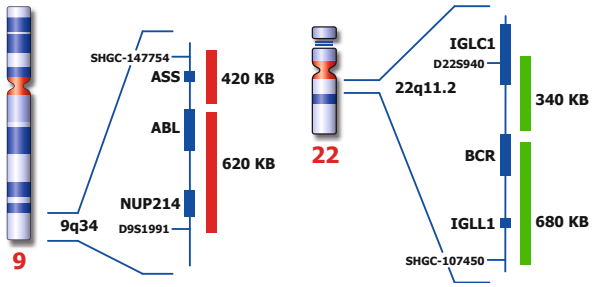


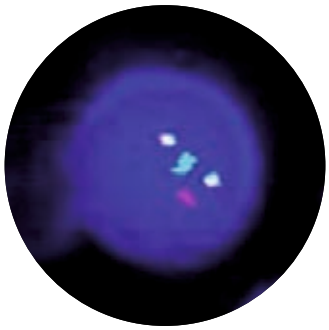
ON BCR/ABL t(9;22), Fusion

The BCR/ABL t(9;22) Fusion is optimized to detect the t(9;22) (q34;q11) reciprocal translocation in a dual-color, dual-fusion assay on metaphase/interphase spreads, blood smears and bone marrow cells.

This probe will also detect cryptic insertions of ABL into the BCR region not detectable by karyotyping and therefore described as Ph-negative.

Cat.# KBI-10005 BCR/ABL t(9;22), Fusion





BCR/ABL t(9;22) Fusion probe hybridized on patient material showing t(9;22) (q34;q11) reciprocal translocation (2RG1R1G).
Image kindly provided by Monika Conchon, São Paulo.

Literature:

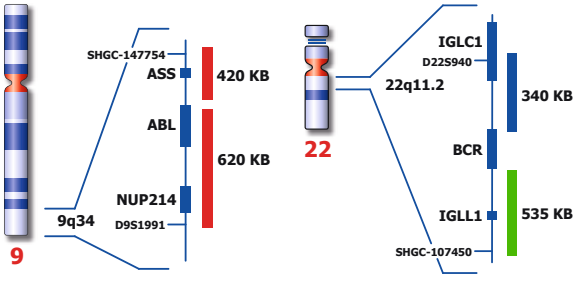
Morris et al, 1990, Blood, 76: 1812-1818.
Dewald et al, 1998, Blood, 91: 3357-3365.
Kolomietz et al, 2001, Blood, 97; 3581-3588.
Huntly et al, 2003, Blood, 102; 1160-1168.
Tkachuk et al., 1990, Science 250, 559-562.

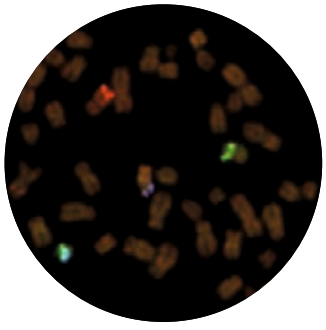
Ordering information	Color	Tests	Cat#
ON BCR/ABL t(9;22) Fusion	red/green	10	KBI-10005
ON BCR/ABL t(9;22) Fusion	red/green	20	KBI-12005

ON BCR/ABL t(9;22), TC, D-Fusion

The BCR/ABL t(9;22), TC, D-Fusion probe is a triple-color, dual-fusion probe build from the same regions as the dual-color, dual-fusion probe, but the proximal BCR region is labeled in blue. Using the triple-color probe allows to distinguish between the derivative chromosome 22, the Philadelphia chromosome, which will be observed as purple (red/blue) color, while the derivative chromosome 9 will show a yellow (red/green) signal.

Cat.# KBI-10006 BCR/ABL t(9;22), TC, D-Fusion





BCR/ABL t(9;22), TC, D-Fusion probe hybridized on patient material showing translocation of distal BCR (1BG1RB1R1G).
Image kindly provided by Prof. Siebert, Kiel.

Literature:

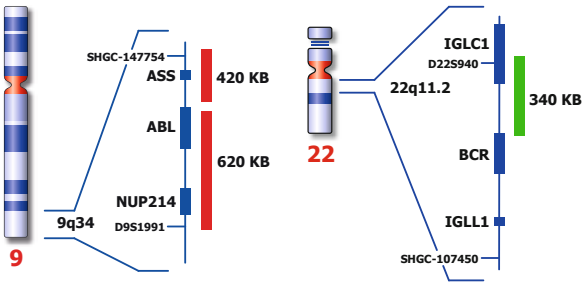
Morris et al, 1990, Blood, 76: 1812-1818.
Dewald et al, 1998, Blood, 91: 3357-3365.
Kolomietz et al, 2001, Blood, 97; 3581-3588.
Huntly et al, 2003, Blood, 102; 1160-1168.
Tkachuk et al., 1990, Science 250, 559-562.

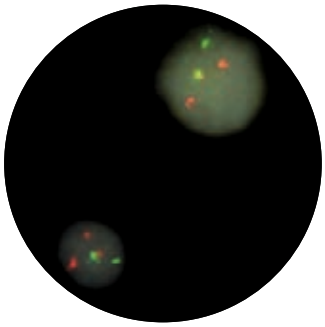
Ordering information	Color	Tests	Cat#
ON BCR/ABL t(9;22) TC, D-Fusion	red/green/blue	10	KBI-10006

ON BCR/ABL t(9;22), DC, S-Fusion, ES

A single-fusion assay is preferably used for the initial screening of CML and ALL patients. Proximal to the breakpoints on chromosome 9q34, this probe will provide an extra signal on the der(9q34) in case of a t(9;22). The Philadelphia chromosome, der(22q), is visualized by the fusion signal.

Cat.# KBI-10008 BCR/ABL t(9;22), Dual-Color, Single-Fusion, Extra Signal





BCR/ABL t(9;22), DC, S-Fusion, ES probe hybridized to patient material showing t(9;22)translocation (1RG1r1R1G).
Material kindly provided by Dr. Balogh, Budapest.

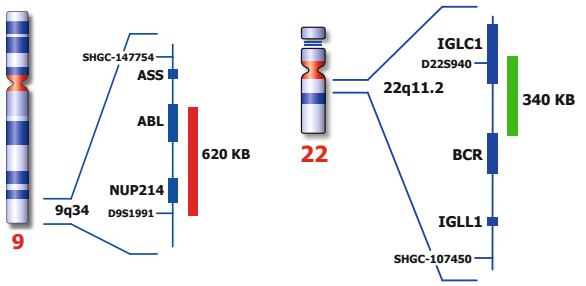
Literature:
Morris et al, 1990, Blood, 76: 1812-1818.
Dewald et al, 1998, Blood, 91: 3357-3365.
Kolomietz et al, 2001, Blood, 97; 3581-3588.
Huntly et al, 2003, Blood, 102; 1160-1168.
Tkachuk et al., 1990, Science 250, 559-562.

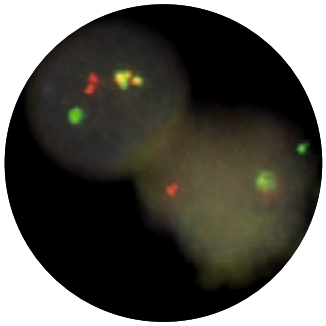
Ordering information	Color	Tests	Cat#
ON BCR/ABL t(9;22) DC, S-Fusion, ES	red/green	10	KBI-10008

ON BCR/ABL t(9;22), DC, S-Fusion

A simple dual-color, single-fusion assay is preferably used for the initial screening of CML and ALL patients. The Philadelphia chromosome, der(22q), is visualized by a fusion signal while the der(9q) shows no signal.

Cat.# KBI-10009 BCR/ABL t(9;22) Dual-Color, Single-Fusion





BCR/ABL t(9;22), DC, S-Fusion probe hybridized to patient material showing t(9;22)translocation (1RG1R1G).
Material kindly provided by Dr. Balogh, Budapest.

Literature:
Morris et al, 1990, Blood, 76: 1812-1818.
Dewald et al, 1998, Blood, 91: 3357-3365.
Kolomietz et al, 2001, Blood, 97; 3581-3588.
Huntly et al, 2003, Blood, 102; 1160-1168.
Tkachuk et al., 1990, Science 250, 559-562.

Ordering information	Color	Tests	Cat#
ON BCR/ABL t(9;22) DC, S-Fusion	red/green	10	KBI-10009

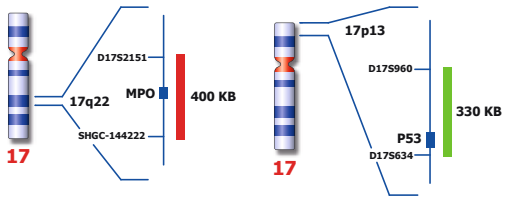
CML secondary chromosomal changes

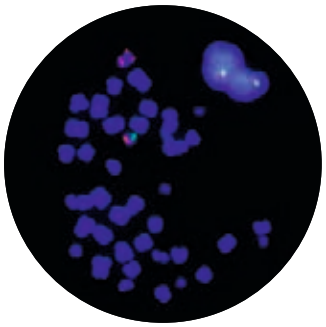
ON p53 (17p13) / MPO (17q22) “ISO 17q”

Isochromosome 17q is the most common isochromosome in cancer. It plays an important role in tumor development and progression. Hematologic malignancies such as chronic myeloid leukemia (CML) with isochromosome 17q carry a poor prognosis. Isochromosome 17q is the most common chromosome abnormality in primitive neuroectodermal tumors and medulloblastoma. Isochromosome 17q is, by convention, symbolized as i(17q).

The p53 (17p13) / MPO (17q22) “ISO 17q” probe is optimized to detect copy numbers of the p53 gene region at 17p13 and MPO gene region at 17q22. In case of i(17q) a signal pattern of three red signals for MPO (17q22) and one signal for p53 at 17p13 is expected.

Cat.# KBI-10011 p53 (17p13) / MPO (17q22) “ISO 17q”





p53 (17p13) / MPO (17q22) "ISO 17q" probe hybridized to peripheral blood of a CLL patient with an isochromosome 17 (3R1G).
Image kindly provided by Dr. Lana Harder, Kiel.

Literature:

Becher et al, 1990, Blood, 75: 1679-1683.
Fioretos et al, 1999, Blood, 94: 225-232.

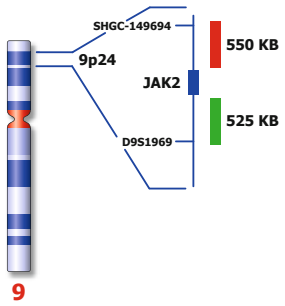
Ordering information	*Color*	*Tests*	*Cat#*
ON p53 (17p13) / MPO (17q22) “ISO 17q”	green/red	10	KBI-10011

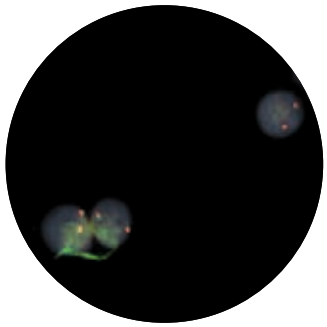
ON JAK2 (9p24) Break

Janus Kinase 2 (JAK2) is a tyrosine kinase involved in cytokine signaling. Mutations and translocations involving the JAK2 gene region are observed in myeloproliferative neoplasms. The common JAK2617V>F point mutation and translocations results in constitutive activation of JAK2. Translocations are described with the following fusion partners: PCM1, BCR, ETV6 (TEL), SSBP2 and 3q21. Patients with the JAK2617V>F point mutation can also exhibit a numerical gain of the gene.

The JAK2 (9p24) Break probe is optimized to detect translocations involving the JAK2 gene region at region 9p24 in a dual-color, split assay on metaphase/interphase spreads. The JAK2 (9p24) Break probe can not be used to detect point mutations, and it has not been optimized to detect gene amplifications.

Cat# KBI-10012 JAK2 (9p24) Break





JAK2 (9p24) Break probe hybridized to bone marrow sample (2RG).

Literature:

Najfeld V et al, 2007, Exp Hematol, 35, 1668-1676.
Smith C et al, 2008, Hum Pathol, 39, 795-810.
Poitras J et al, 2008, Genes Chromosomes Cancer, 47, 884-889.

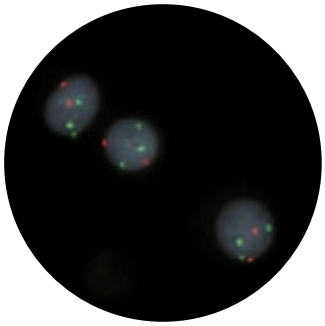
Ordering information	*Color*	*Tests*	*Cat#*
ON JAK2 (9p24) Break	red/green	10	KBI-10012

SE 8 (D8Z1)
SE 7 (D7Z1) / SE 8 (D8Z1)

Gain of chromosome 8 is the most common secondary chromosomal aberration in CML (approx. 34%).

Cat.# KBI-20008 SE 8 (D8Z1)
Cat.# KBI-20031 SE 7 (D7Z1) / SE 8 (D8Z1)

See description under Satellite Enumeration probes on page 94.



SE 7 / SE 8 showing trisomy 8.
Material kindly provided by Dr. Balogh, Budapest.

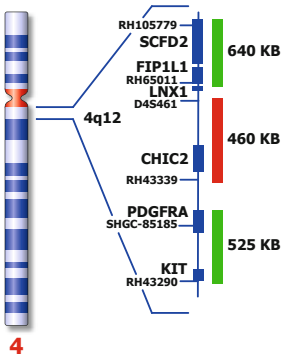
Ordering information	Color	Tests	Cat#
SE 8 (D8Z1)	red/green	10	KBI-20008
SE 7 (D7Z1) / SE 8 (D8Z1)	red/green	10	KBI-20031

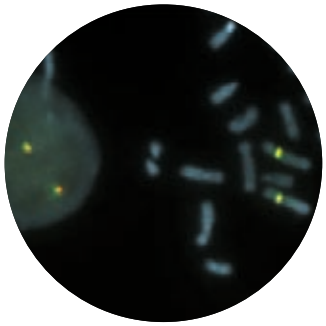
Other Myeloproliferative Diseases:

ON FIP1L1-CHIC2-PDGFRA (4q12) Del, Break

Idiopathic hypereosinophilic syndrome (HES) and chronic eosinophilia leukemia (CEL) represent the most recent additions to the list of molecularly defined chronic myeloproliferative disorders. A novel tyrosine kinase that is generated from fusion of the Fip1-like 1 (FIP1L1) and PDGFRα (PDGFRA) genes has been identified as a therapeutic target for imatinib mesylate in hypereosinophilic syndrome (HES). This fusion results from an approximately 800-kb interstitial chromosomal deletion that includes the cysteine-rich hydrophobic domain 2 (CHIC2) locus. The FIP1L1-CHIC2-PDGFRA probe is optimized to detect the CHIC2 deletion at 4q12 associated with the FIP1L1/PDGFRA fusion in a Dual-Color, split assay. It also allows the detection of translocation involving the FIP1L1 and PDGFRA region. However, chromosome 4 polyploidy may provide additional signals not associated with a translocation involving 4q12.

Cat.# KBI-10003 FIP1L1-CHIC2-PDGFRA (4q12) Del, Break





FIP1L1-CHIC2-PDGFRA (4q12) Del, Break probe hybridized to a normal interphase/metaphase (2RG).

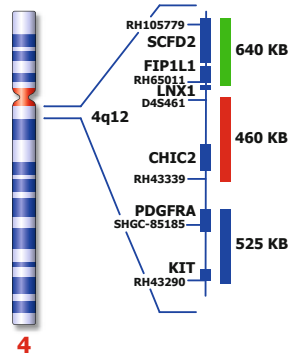
Literature:
Cools et al, N Engl J Med, 2003, 348, 1201-1214.
Godlib et al, Blood, 2004, 103, 2879-2891.

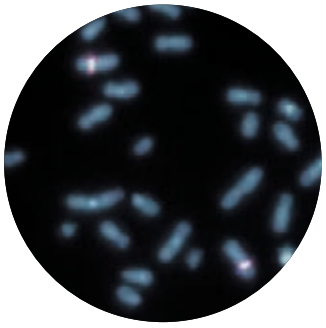
Ordering information	Color	Tests	Cat#
ON FIP1L1-CHIC2-PDGFRA (4q12) Del, Break	red/green	10	KBI-10003

ON FIP1L1-CHIC2-PDGFRA (4q12) Del, Break, TC

The FIP1L1-CHIC2-PDGFRA triple-color probe is optimized to detect the CHIC2 deletion at 4q12 associated with the FIP1L1/PDGFRA fusion in a triple-color, split assay. It also allows the detection of translocation involving the FIP1L1 and PDGFRA region.

Cat.# KBI-10007 FIP1L1-CHIC2-PDGFRA (4q12) Del, Break, Triple-Color





FIP1L1-CHIC2-PDGFRA (4q12) Del, Break, TC probe hybridized to a normal metaphase (2BRG).

Literature:

Cools et al, 2003, N Engl J Med, 348: 1201-1214.
Griffin et al, 2003, PNAS, 100: 7830-7835.
Gotlib et al, 2004, Blood, 103; 2879-2891.

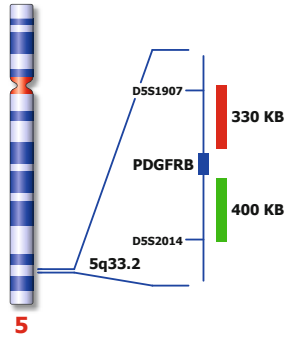
Ordering information	*Color*	*Tests*	*Cat#*
ON FIP1L1-CHIC2-PDGFRA (4q12) Del, Break, TC	red/green/blue	10	KBI-10007

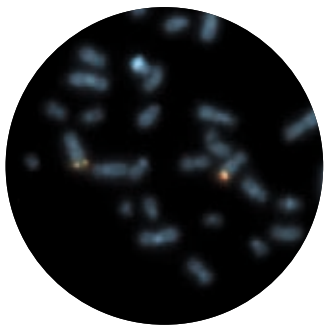
ON PDGFRB (5q33) Break

PDGFRB activation has been observed in patients with chronic myelomonocytic leukemia/atypical chronic myeloid leukemia and has been associated with 11 translocation partners, the best known is the ETV6 gene on 12p13, causing a t(5;12) translocation. Cytogenetic responses are achieved with imatinib in patients with PDGFRB fusion positive, BCR/ABL negative CMPDs.

The PDGFRB probe is optimized to detect translocations involving the PDGFRB region at 5q33 in a dual-color, split assay.

Cat.# KBI-10004 PDGFRB (5q33) Break





PDGFRB (5q33) Break probe hybridized to a normal metaphase (2RG).

Literature:

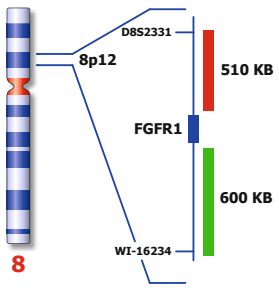
Wlodarska et al, 1997, Blood, 89: 1716-1722.
Wilkinson et al, 2003, Blood, 102: 4287-419.

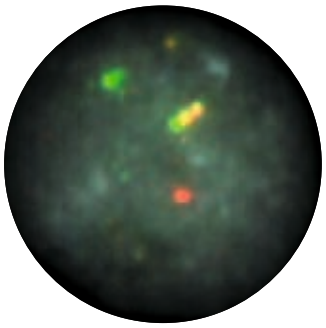
Ordering information	*Color*	*Tests*	*Cat#*
ON PDGFRB (5q33) Break	red/green	10	KBI-10004

ON FGFR1 (8p12) Break

FGFR1 has been implicated in the tumorigenesis of haematological malignancies, where it is frequently involved in balanced chromosomal translocations, including cases of chronic myeloid leukaemia (BCR-FGFR1 fusion) and the 8p11 myeloproliferative syndrome/stem cell leukaemia–lymphoma syndrome, which is characterized by myeloid hyperplasia and non-Hodgkin's lymphoma with chromosomal translocations fusing several genes, the most common being a fusion between ZNF198 and FGFR1.

Cat.# KBI-10737 FGFR1 (8p12) Break





FGFR1 (8p12) Break probe hybridized to patient material showing a break at 8p12 (1RG1R1G).

Literature:
Smedley et al, 1998, Hum Mol Genet. 7; 627-642.
Sohal et al, 2001, Genes Chrom. Cancer 32; 155-163.
Kwak et al, J Clin Oncol., 27(26):4247-53.

Ordering information	*Color*	*Tests*	*Cat#*
ON FGFR1 (8p12) Break	red/green	10	KBI-10737

Chronic Lymphocytic Leukemia (CLL)

CLL accounts for about 30% of all leukemias in Europe and the USA. Distinct clonal chromosomal abnormalities can be identified in up to 90% of CLL cases of the B-cell lineage. By FISH the most common chromosomal changes in CLL and their frequencies have been identified as shown in the table below.

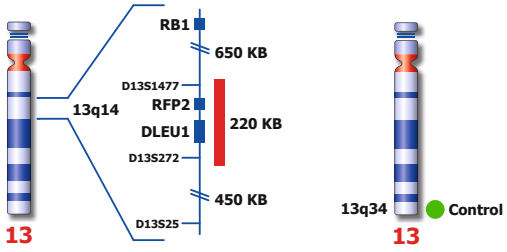
Del(13q14)	55%
Del(11q)	18%
Trisomy 12q	16%
Del(17p)	7%
Del(6q)	6%
Trisomy 8q	5%
t(14q32)	4%
Trisomy 3q	3%

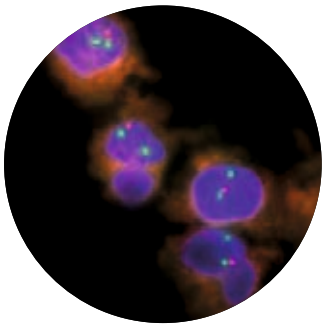
ON DLEU (13q14) / 13qter

Deletions of chromosome 13q14 have been reported not only in CLL but in a variety of human tumors, including other types of lymphoid and myeloid tumors, as well as prostate, head and neck, and non-small cell lung cancers. The deletion of 13q may be limited to a single locus (13q14), or accompanied with the loss of a larger interstitial region of the long arm of chromosome 13. A minimal critical region of 400 kb has been described containing the DLEU1, DLEU2 and RFP2 genes.

The DLEU (13q14) specific DNA probe is optimized to detect copy numbers of the DLEU gene region at 13q14. The 13qter (13q34) region is included to facilitate chromosome identification.

Cat.# KBI-10102 DLEU (13q14) / 13qter





DLEU (13q14) / 13qter probe hybridized to patient material showing a 13q14 deletion (1R2G).
Image kindly provided by Dr. Dastugue, Toulouse.

Literature:

Wolf et al, 2001, Hum Mol Genet, 10: 1275-1285.
Corcoran et al, 1998, Blood, 91: 1382-1390.

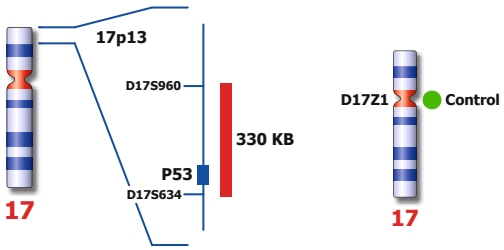
Ordering information	*Color*	*Tests*	*Cat#*
ON DLEU (13q14) / 13qter	red/green	10	KBI-10102

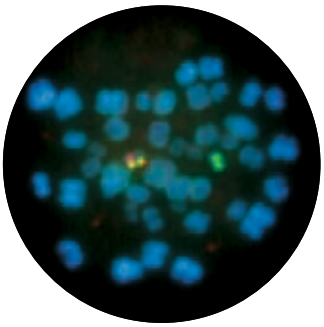
ON p53 (17p13) / SE 17

The p53 tumor suppressor gene at 17p13, has been shown to be implicated in the control of normal cellular proliferation, differentiation, and apoptosis. Allelic loss, usually by deletion, and inactivation of p53 have been reported in numerous tumor types and are associated with poor prognosis in CLL.

The p53 (17p13) specific DNA probe is optimized to detect copy numbers of the p53 gene region at 17p13. The chromosome 17 satellite enumeration probe (SE 17) at D17Z1 is included to facilitate chromosome identification.

Cat.# KBI-10112 p53 (17p13) / SE 17





p53 (17p13) / SE 17 probe hybridized to patient material showing a 17p13 deletion at the p53 gene region (1R2G).

Literature:

Amiel A et al, 1997, Cancer Gener.Cytogenet,, 97; 97-100.
Drach J et al, 1998, Blood, 92; 802-809.

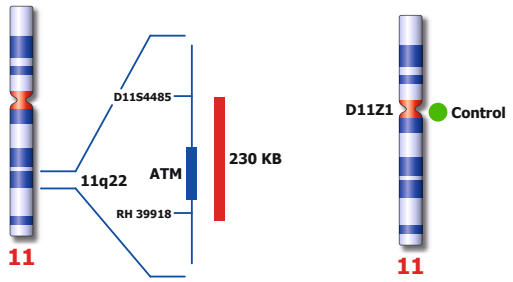
Ordering information	*Color*	*Tests*	*Cat#*
ON p53 (17p13) / SE 17	red/green	10	KBI-10112
ON p53 (17p13) / SE 17	red/green	20	KBI-12112

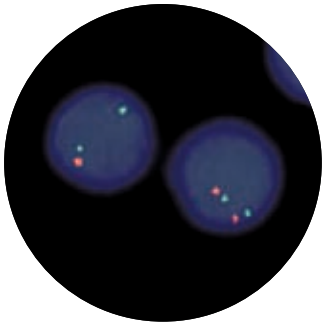
ON ATM (11q22) / SE 11

Chromosome 11q22.3-23.1 deletions involving the ataxia-teleangiectasia mutated (ATM) locus are detected at diagnosis in 15-20% of cases of B-cell chronic lymphocytic leukemia (CLL) and are associated with a relatively aggressive disease. Loss of the 11q22-23 region, where the ataxia-telangiectasia mutated (ATM) gene is located, is also one of the most frequent secondary chromosomal aberrations in mantle cell lymphoma.

The ATM (11q22.3) specific DNA probe is optimized to detect copy numbers of the ATM gene region at region 11q22.3. The chromosome 11 satellite enumeration (SE 11) at D11Z1 probe is included to facilitate chromosome identification.

Cat.# KBI-10103 ATM (11q22) / SE 11





ATM (11q22) / SE 11 hybridized to patient material showing a 11q22 deletion at the ATM gene region (1R2G).
Image kindly provided by Dr. Wenzel, Basel.

Literature:
Doehner et al, 1997, Blood, 89: 2516-2522.
Bigoni et al, 1997, Leukemia, 11: 1933-1940.

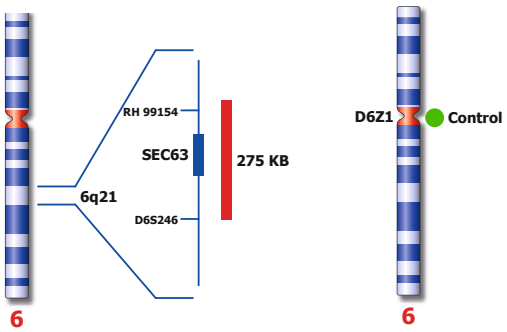
Ordering information	Color	Tests	Cat#
ON ATM (11q22) / SE 11	red/green	10	KBI-10103

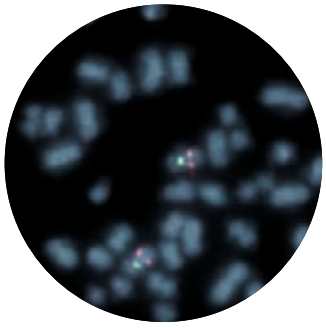
ON 6q21 / SE 6

Deletions affecting the long arm of chromosome 6 (6q) are among the most commonly observed chromosomal aberrations in lymphoid malignancies and have been identified as an adverse prognostic factor in subsets of tumors including CLL. A minimal deletion region has been identified within a 2-megabase segment of 6q21, between D6S447 and D6S246. The SEC63 gene is located within this critical region.

The 6q21 specific DNA probe is optimized to detect copy numbers of 6q at region 6q21.The chromosome 6 satellite enumeration probe (SE 6) at D6Z1 is included to facilitate chromosome identification.

Cat.# KBI-10105 6q21 / SE 6





6q21 / SE 6 probe hybridized to a normal metaphase (2R2G).

Literature:
Sherratt et al, 1997, Chromosome Res, 5: 118-124.
Zhang et al, 2000, Genes Chrom Cancer, 27: 52-58.

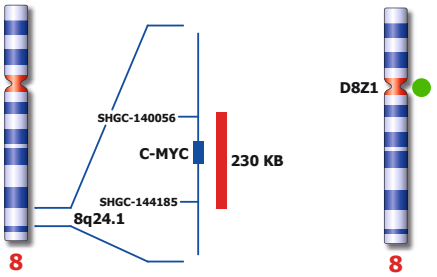
Ordering information	Color	Tests	Cat#
ON 6q21 / SE 6	red/green	10	KBI-10105

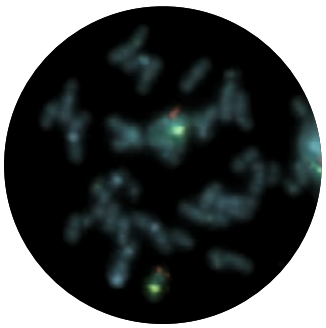
ON C-MYC (8q24) / SE 8

The C-MYC gene produces an oncogenic transcription factor that affects diverse cellular processes involved in cell growth, cell proliferation, apoptosis and cellular metabolism. The C-MYC oncogene has been shown to be amplified in many types of human cancer such as bladder, breast and cervical. Amplification at 8q24 including C-MYC is also observed in 5% of CLL patients. C-MYC is also the prototype for oncogene activation by chromosomal translocation.

The C-MYC (8q24) specific DNA probe is optimized to detect copy numbers of the C-MYC gene region at 8q24. The chromosome 8 satellite enumeration probe (SE 8) at D8Z1 is included to facilitate chromosome identification.

Cat.# KBI-10106 C-MYC (8q24) / SE 8





C-MYC (8q24) / SE 8 hybridized to a normal metaphase (2R2G).

Literature:
Greil et al, 1991, Blood, 78: 180-191.
Note:
This probe should not be used to detect translocations involving C-MYC.

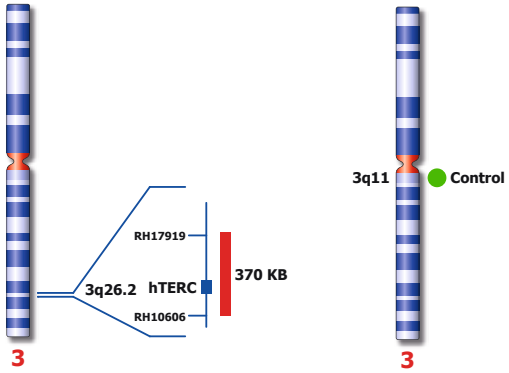
Ordering information	*Color*	*Tests*	*Cat#*
ON C-MYC (8q24) / SE 8	red/green	10	KBI-10106

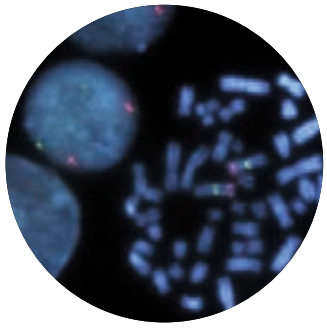
ON hTERC (3q26) / 3q11

Amplification of the 3q26-q27 has a high prevalence in cervical, prostate, lung, and squamous cell carcinoma. This amplification can also be found to a lesser extent in CLL patients. The minimal region of amplification was refined to a 1- to 2-Mb genomic segment containing several potential cancer genes including hTERC, the human telomerase RNA gene.

The hTERC (3q26) specific DNA probe is optimized to detect copy numbers of the hTERC gene region at region 3q26. The 3q11 region probe is included to facilitate chromosome identification.

Cat.# KBI-10110 hTERC (3q26) / 3q11





hTERC (3q26) / 3q11 probe hybridized to a normal interphase/ metaphase (2R2G).

Literature:
Arnold et al, 1996, Genes Chrom Cancer, 16: 46-54.
Soder et al, 1997, Oncogene, 14: 1013-1021.

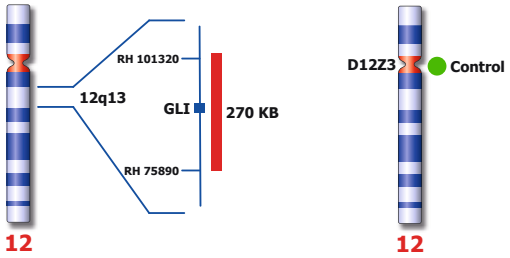
Ordering information	*Color*	*Tests*	*Cat#*
ON hTERC (3q26) / 3q11	red/green	10	KBI-10110

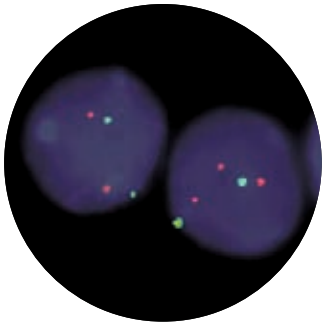
ON GLI (12q13) / SE 12

Trisomy 12 is the most common numerical chromosomal aberration in patients with B-cell chronic lymphocytic leukemia (B-CLL). Partial trisomy 12 of the long arm of chromosome 12 consistently includes a smaller region at 12q13-15 and has been observed in CLL and several other tumors. A number of loci located close to either MDM2 or CDK4/SAS, including the genes GADD153, **GLI**, RAP1B, A2MR, and IFNG, were found to be coamplified.

The GLI (12q13) specific DNA probe is optimized to detect copy numbers of the GLI gene region at region 12q13. The chromosome 12 satellite enumeration probe (SE 12) D12Z3 is included to facilitate chromosome identification.

Cat.# KBI-10104 GLI (12q13) / SE 12





GLI (12q13) / SE 12 hybridized to patient material showing GLI (12q13) amplification (3R2G).
Image kindly provided by Dr. Wenzel, Basel.

Literature:
Merup et al, 1997, Eur J Haematol, 58: 174-180.
Dierlamm et al., 1997, Genes Chrom Cancer, 20: 155-166.

Ordering information	Color	Tests	Cat#
ON GLI (12q13) / SE 12	red/green	10	KBI-10104

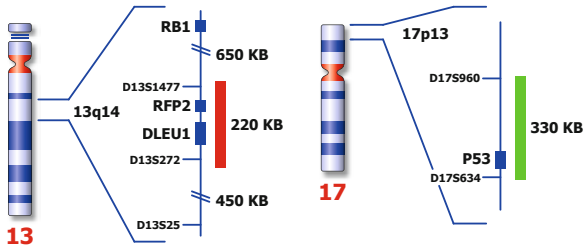
CLL probe combinations

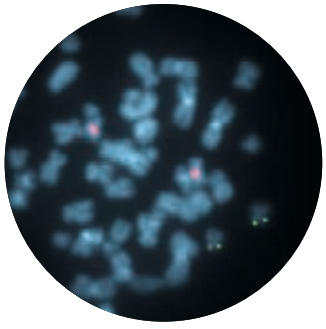
Most of the CLL probes are also available as combinations covering two critical loci in one hybridization. This is of particular interest if patient material is limited. The disadvantage is that no internal control is added. The following CLL probe combinations are available:

ON DLEU (13q14) / p53 (17p13)

Deletion of DLEU at 13q14 indicates a rather good prognosis, deletion of p53 at 17p13 is associated with poor prognosis.

Cat.# KBI-10113 DLEU (13q14) / p53 (17p13)





DLEU (13q14) / p53 (17p13) hybridized to a normal metaphase (2R2G).

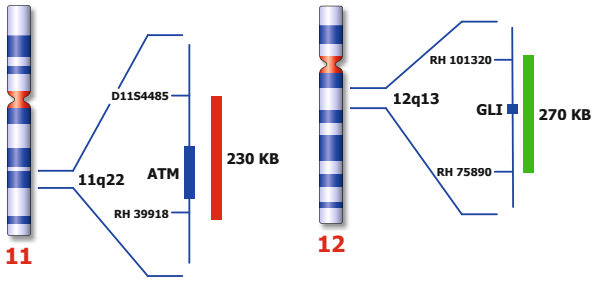
Literature:
Amiel A et al, 1997, Cancer Gener.Cytogenet, 97; 97-100.
Drach J et al, 1998, Blood, 92; 802-809.
Stilgenbauer S et al, 1998, Oncogene, 16; 1891 – 1897.
Wolf S et al, 2001, Hum. Molec. Genet., 10; 1275-1285.

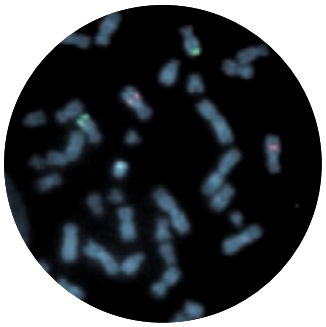
Ordering information	Color	Tests	Cat#
ON DLEU (13q14) / p53 (17p13)	red/green	10	KBI-10113

ON ATM (11q22) / GLI (12q13)

Deletion of ATM at 11q22-q23 indicates a rather poor prognosis, amplification of GLI at 12q13 is associated with an intermediate prognosis.

Cat.# KBI-10108 ATM (11q22) / GLI (12q13)



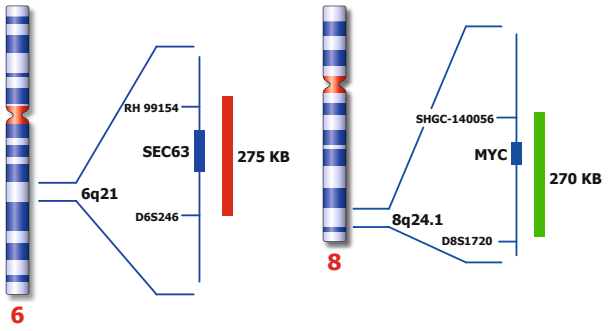


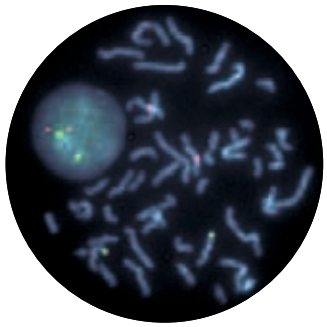
ATM (11q22) / GLI (12q13) hybridized to a normal metaphase (2R2G).

ON 6q21 / MYC (8q24)

Deletion of 6q21 indicates an intermediate risk category, amplification of MYC at 8q24 is associated with poor prognosis.

Cat.# KBI-10117 6q21 / MYC (8q24)





6q21 / MYC (8q24) hybridized to a normal interphase/ metaphase (2R2G).

Literature:

Döhner H et al, 1997, Blood, 7; 2516-2522.
Boultwood J, 2001, J. Clin. Pathol., 54; 512-516.
Dierlamm J et al, 1998, Genes Chromosomes Cancer, 20; 155-166.
Döhner H at al, 1999, J. Molec. Med., 77; 266-281.

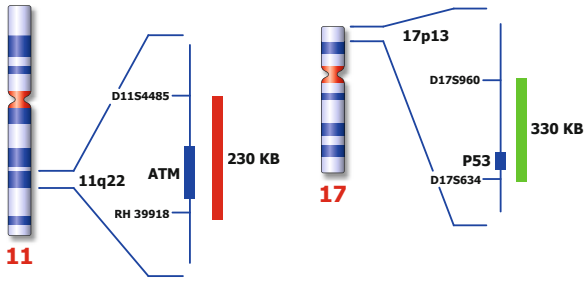
Ordering information	*Color*	*Tests*	*Cat#*
ON ATM (11q22) / GLI (12q13)	red/green	10	KBI-10108

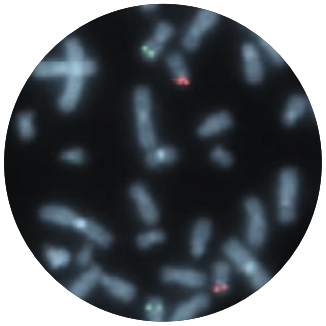
Ordering information	*Color*	*Tests*	*Cat#*
ON 6q21 / MYC (8q24)	red/green	10	KBI-10117

ON p53 (17p13) / ATM (11q22)

Deletion of p53 and ATM are both indicating poor prognosis in CLL.

Cat.# KBI-10114 p53 (17p13) / ATM (11q22)





p53 (17p13) / ATM (11q22) hybridized to a normal metaphase (2R2G).

Ordering information	Color	Tests	Cat#
ON p53 (17p13) / ATM (11q22)	red/green	10	KBI-10114

Other relevant CLL probes:

ON IGH (14q32) Break

Cat.# KBI-10601 IGH (14q32) Break

See description under Lymphoma on page 44.

Ordering information	Color	Tests	Cat#
ON IGH (14q32) Break	red/green	10	KBI-10601

SE 12 (D12Z3)

Cat.# KBI-20012 SE 12 (D12Z3)

See description under Satellite Enumeration probes on page 94.

Ordering information	Color	Tests	Cat#
SE 12 (D12Z3)	red/green	10	KBI-20012

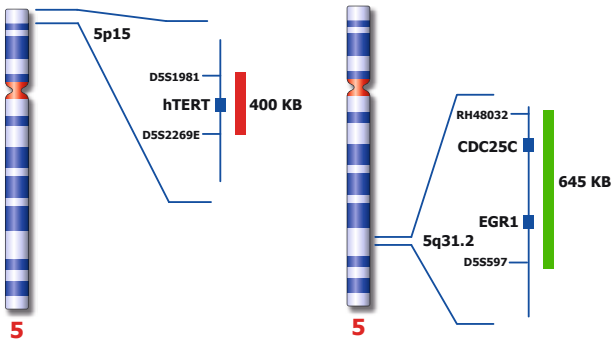
Myelodysplastic Syndromes (MDS)

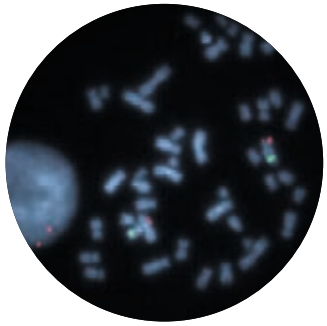
The myelodysplastic syndromes (MDS) are a heterogeneous group of hematopoietic disorders characterized in most patients by peripheral blood cytopenia with hypercellular bone marrow and dysplasia of the cellular elements. Cytogenetic studies play a major role in confirmation of diagnosis and prediction of clinical outcome in MDS, and have contributed to the understanding of its pathogenesis. Clonal chromosomal abnormalities are detected by routine karyotyping techniques in 40%–70% of cases of de novo MDS, and 95% of cases of therapy-related MDS.

ON hTERT (5p15) / 5q31

The hTERT / 5q31 dual-color probe can be used to detect deletions involving band 5q31 in MDS and AML. The 5q- specific DNA probe is optimized to detect copy numbers at the CDC25C/EGR1 gene region at 5q31. The hTERT gene region at 5p15 is included to facilitate chromosome identification.

Cat.# KBI-10208 hTERT (5p15) / 5q31





hTERT (5p15) / 5q31 probe hybridized to a normal interphase/ metaphase (2R2G).

Literature:
Zhao et al, 1997, PNAS, 94; 6948-6053.
Horrigan et al, 2000, Blood, 95; 2372-2377.

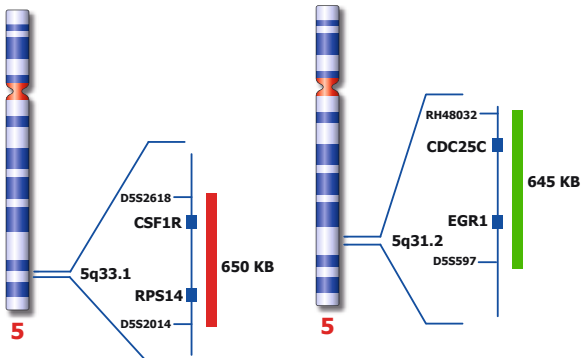
Ordering information	*Color*	*Tests*	*Cat#*
ON hTERT (5p15) / 5q31	red/green	10	KBI-10208

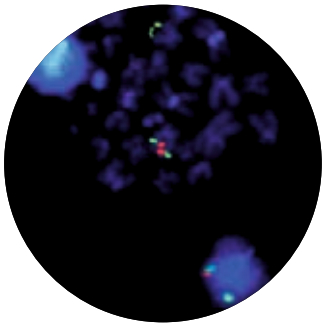
ON MDS 5q- (5q31; 5q33)

The presence of del(5q), either as the sole karyotypic abnormality or as part of a more complex karyotype, has distinct clinical implications for myelodysplastic syndromes (MDS) and acute myeloid leukemia. Interstitial 5q deletions are the most frequent chromosomal abnormalities in MDS and are present in 10% to 15% of MDS patients. Two different critical regions are described, one at 5q31-q33 containing the CSF1R and RPS14 gene regions, characteristic for the '5q-' syndrome, and a more proximal located region at 5q13-q31 containing the CDC25C and EGR1 gene regions.

The 5q- specific DNA probe is optimized to detect copy numbers at the CDC25C/EGR1 gene region at 5q31 and the CSF1R/RPS14 gene region at 5q33 simultaneously in a dual-color assay.

Cat.# KBI-10209 MDS 5q- (5q31; 5q33)





MDS 5q- (5q31; 5q33) probe hybridized to patient material showing a 5q33 deletion (1R2G).
Image kindly provided by Dr. Mohr, Dresden.

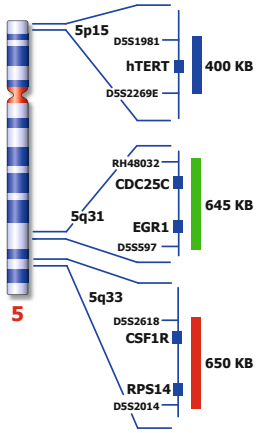
Literature:
Boultwood J e.a., Blood 2002; 99: 4638-4641.
Zhao N e.a., PNAS 1997; 94: 6948-6953.
Wang e.a., Haematologica 2008; 93: 994-1000 .
Ebert BL e.a., Nature 2008: 451: 335-339.
Mohamedali A and Mufti GJ, Brit J Haematol 2008; 144: 157-168.

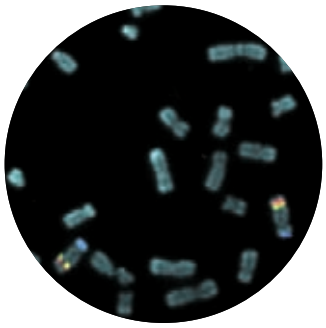
Ordering information	Color	Tests	Cat#
ON MDS 5q- (5q31; 5q33)	red/green	10	KBI-10209

ON MDS 5q- (5q31; 5q33) / hTERT (5p15) TC

The 5q- specific DNA probe is optimized to detect copy numbers at the CDC25C/EGR1 gene region at 5q31 and the CSF1R/RPS14 gene region at 5q33 simultaneously in a dual-color assay. The triple-color probe provides in addition to the two critical regions a control in blue targeting the hTERT gene region at 5p15.

Cat.# KBI-10210 MDS 5q- (5q31; 5q33) / hTERT (5p15), Triple-Color





MDS 5q- (5q31; 5q33) / hTERT (5p15) probe hybridized to a normal metaphase (2R2G2B).

Literature:
Boultwood J e.a., Blood 2002; 99: 4638-4641.
Zhao N e.a., PNAS 1997; 94: 6948-6953.
Wang e.a., Haematologica 2008; 93: 994-1000.
Ebert BL e.a., Nature 2008: 451: 335-339.
Mohamedali A and Mufti GJ, Brit J Haematol 2008; 144: 157-168.

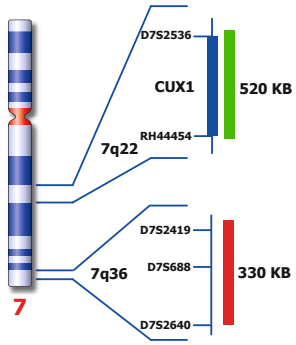
Ordering information	Color	Tests	Cat#
ON MDS 5q- (5q31; 5q33) / hTERT (5p15) TC	red/green/blue	10	KBI-10210

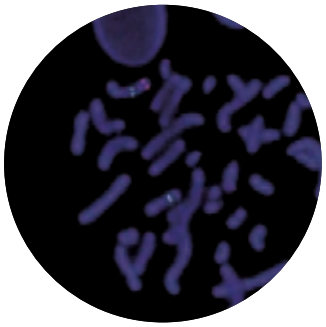
ON MDS 7q- (7q22; 7q36)

Loss of a whole chromosome 7 or a deletion of the long arm, del(7q), are recurring abnormalities in malignant myeloid diseases. Most deletions are interstitial and there are two distinct deleted segments of 7q. The majority of patients have proximal breakpoints in bands q11-22 and distal breakpoints in q31-36. The CCAAT displacement protein CUX1 gene region is located in the 7q22 critical region.

The 7q- specific DNA probe is optimized to detect copy number of 7q at 7q22 and at 7q36 simultaneously in a dual-color assay

Cat.# KBI-10202 MDS 7q- (7q22; 7q36)





MDS 7q- (7q22; 7q36) hybridized to patient material showing a 7q36 deletion (1R2G).
Image kindly provided by Prof. Jauch, Heidelberg.

Literature:
LeBeau et al., 1996, Blood, 88: 1930-1935.
Doehner et al, 1998, Blood, 92: 4031-4035.

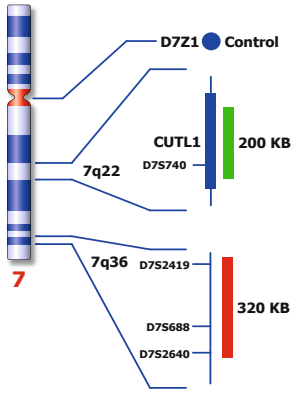
Ordering information	*Color*	*Tests*	*Cat#*
ON MDS 7q- (7q22; 7q36)	red/green	10	KBI-10202

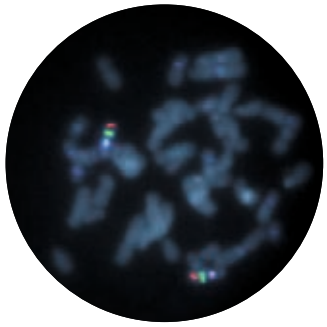
ON MDS 7q- (7q22; 7q36) / SE 7 TC

The 7q- specific DNA probe is optimized to detect copy number of 7q at 7q22 and at 7q36 simultaneously in a dual-color assay.

The chromosome 7 satellite enumeration probe (SE 7) at D7Z1 in blue is included to facilitate chromosome identification.

Cat.# KBI-10207 MDS 7q (7q22; 7q36) / SE 7, Triple-Color





MDS 7q (7q22; 7q36) / SE 7 TC probe hybridized to a normal metaphase (2R2G2B).

Literature:
LeBeau et al., 1996, Blood, 88: 1930-1935.
Doehner et al, 1998, Blood, 92: 4031-4035.

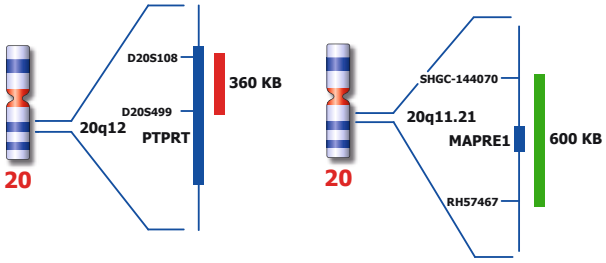
Ordering information	*Color*	*Tests*	*Cat#*
ON MDS 7q- (7q22; 7q36) / SE7 TC	red/green/blue	10	KBI-10207

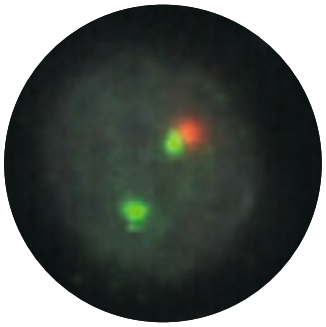
ON MDS 20q- (PTPRT 20q12) / 20q11

Acquired deletions of the long arm of chromosome 20 are found in several hematologic conditions and particularly in the myeloproliferative disorders (MPD) and myelodysplastic syndromes and acute myeloid leukemia (MDS/AML). A minimal critical region deleted in MPD and MDS has been identified at 20q12 which includes a protein tyrosine phosphatase receptor gene (PTPRT).

The 20q- (PTPRT, 20q12) specific DNA probe is optimized to detect copy numbers of 20q at region 20q12. A 20q11 region specific probe is included to facilitate chromosome identification.

Cat.# KBI-10203 MDS 20q- (PTPRT 20q12) / 20q11





MDS 20q- (PTPRT 20q12) / 20q11 probe hybridized to patient material showing 20q- deletion (1R2G).
Material kindly provided by Labdia Labordiagnostik, Vienna.

Literature:
Bench et al, 2000, Oncogene, 19: 3902-3913.
Asimakopoulos et al, 1994, Blood, 84: 3086-3094.

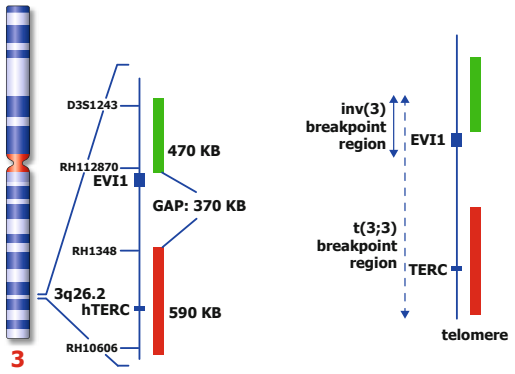
Ordering information	Color	Tests	Cat#
ON 20q- (PTPRT 20q12) / 20q11	red/green	10	KBI-10203

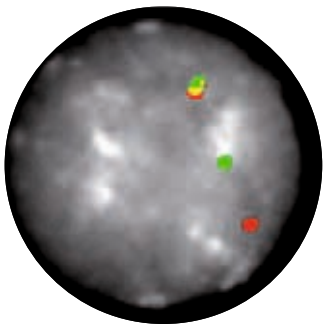
ON EVI t(3;3); inv(3) (3q26) Break

The inv(3)(q21;q26) is a recurrent cytogenetic aberration of myeloid malignancy associated with fusion of EVI1 and RPN1 and a poor disease prognosis. Genomic breakpoints in 3q26 are usually located proximal to the EVI1 locus, spanning a region of several hundred kilobases. Other recurrent and sporadic rearrangements of 3q26 also cause transcriptional activation of EVI1 including the translocations t(3;3)(q21;q26) and t(3;21)(q26;q22). Breakpoints in the latter rearrangements span a wider genomic region of over 1 megabase encompassing sequences distal to EVI1 and neighboring gene MDS1.

The EVI t(3;3) inv(3) Break, dual-color probe is optimized to detect the inversion of chromosome 3 involving the EVI1 gene region at 3q26 in a dual-color, split assay on metaphase/interphase spreads, blood smears and bone marrow cells.

Cat.# KBI-10204 EVI t(3;3); inv(3) (3q26) Break





EVI t(3;3);inv(3) (3q26) Break probe hybridized to patient material showing a rearrangement involving the EVI gene region at 3q26 (1RG1R1G). Image kindly provided by Dr. Reed, London.

Literature:
Levy et al, 1994, Blood, 83: 1348-1354.
Wieser et al, 2003, Haematologica, 88: 25-30.
Melo et al, 2007, Leukemia, 22, 434-437.

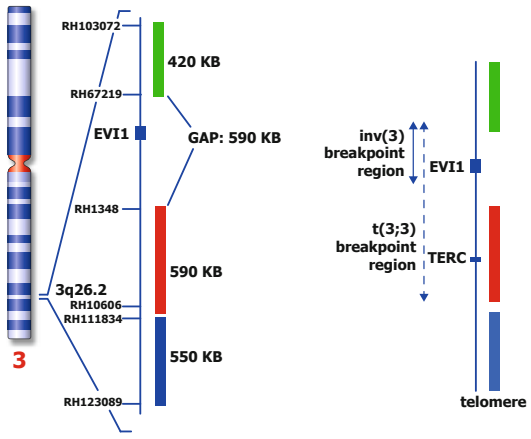
Note: In t(3;3) the breakpoint cluster can span 1.3 Mb region. The described probe set will therefore provide false negative results in cases with very distal breakpoints.

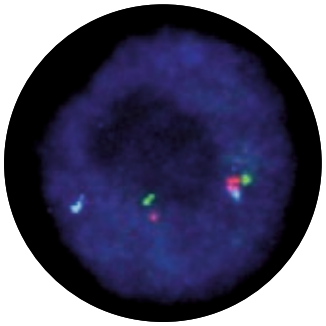
Ordering information	Color	Tests	Cat#
ON EVI t(3;3); inv(3) (3q26) Break	red/green	10	KBI-10204

ON EVI t(3;3); inv(3), EVI (3q26) Break, TC

The EVI t(3;3) inv(3) Break, triple-color probe is optimized to detect the inversion of chromosome 3 involving the EVI gene region at 3q26 in a dual-color, split assay on metaphase/ interphase spreads, blood smears and bone marrow cells. By using a third color breakpoint variations can also be easily observed.

Cat.# KBI-10205 EVI t(3;3); inv(3) (3q26), Triple-Color





EVI t(3;3); inv(3) (3q26) TC probe hybridized to patient material showing a rearrangement involving the EVI gene region at 3q26 (1RGB1B1RG). Image kindly provided by Prof. Jauch, Heidelberg.

Literature:

Levy et al, 1994, Blood, 83: 1348-1354.
Wieser et al, 2003, Haematologica, 88: 25-30.
Melo et al, 2007, Leukemia, 22, 434-437.

Ordering information	*Color*	*Tests*	*Cat#*
ON EVI t(3;3); inv(3) (3q26) Break, TC	red/green/blue	10	KBI-10205

Acute Myeloid Leukemia (AML)

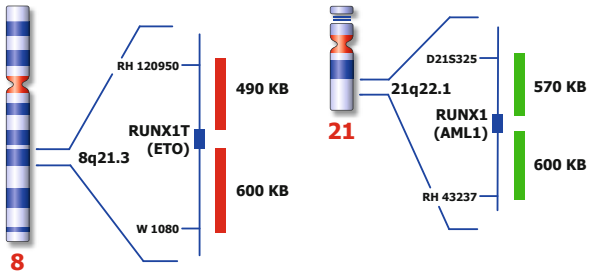
At least 80% of patients with acute myeloid leukemia (AML) have an abnormal karyotype. Cytogenetic analysis provides some of the strongest prognostic information available, predicting outcome of both remission induction and postremission therapy. Abnormalities which indicate a good prognosis include t(8;21), inv(16), and t(15;17). Patients with AML that is characterized by deletions of the long arms or monosomies of chromosomes 5 or 7; by translocations or inversions of chromosome 3, t(6;9), t(9;22); or by abnormalities of chromosome 11q23 have particularly poor prognoses with chemotherapy.

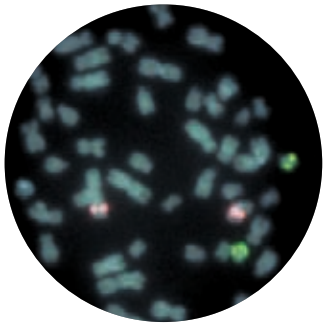
ON AML/ETO t(8;21) Fusion

t(8;21)(q21;q22) is the most frequently observed karyotypic abnormality associated with acute myeloid leukemia (AML), especially in FAB M2. As a consequence of the translocation the AML1 (CBFA2, RUNX1) gene in the 21q22 region is fused to the ETO (MTG8 , RUNX1T) gene in the 8q21 region, resulting in one transcriptionally active gene on the 8q-derivative chromosome.

The AML/ETO t(8;21)(q21;q22) specific DNA probe is optimized to detect the reciprocal translocation t(8;21) in a dual-color, dual-fusion assay.

Cat.# KBI-10301 AML/ETO t(8;21) Fusion





AMl/ETO t(8;21) Fusion probe hybridized to a normal metaphase (2R2G).

Literature:

Sacchi et al, 1995, Genes Chrom Cancer, 79: 97-103.
Hagemeijer et al, 1998, Leukemia, 12: 96-101.

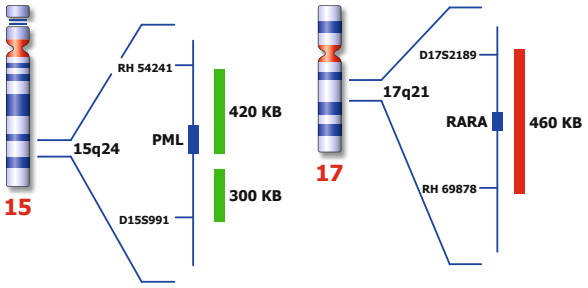
Ordering information	Color	Tests	Cat#
ON AML/ETO t(8;21) Fusion	red/green	10	KBI-10301

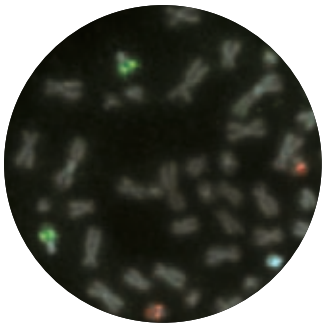
ON PML/RARA t(15;17) Fusion

A structural rearrangement involving chromosomes 15 and 17 in acute promyelocytic leukemia (APL) was first recognized in 1977. The critical junction is located on the der(15) chromosome and consists of the 5' portion of PML fused to virtually all of the RARA gene. The PML/RARA fusion protein interacts with a complex of molecules known as nuclear co-repressors and histone deacetylase. This complex binds to the fusion protein and blocks the transcription of target genes. Other less common variant translocations fuse the RARA gene on 17q21 to the PLZF, NPM, NUMA, and STAT5b genes, respectively.

The PML/RARA t(15;17) specific DNA probe is optimized to detect the reciprocal translocation t(15;17) (q24;q21) in a dual-color, dual-fusion assay.

Cat.# KBI-10302 PML/RARA t(15,17) Fusion





PML/RARA t(15,17) Fusion probe hybridized to a normal metaphase (2R2G).

Literature:

Schad et al, 1994, Mayo Clin Proc, 69: 1047-1053.
Brockman et al, 2003, Cancer Genet Cytogenet, 145: 144-151.

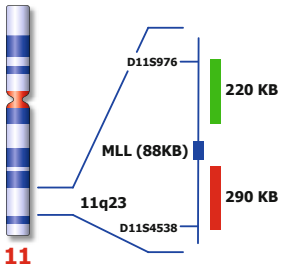
Ordering information	Color	Tests	Cat#
ON PML/RARA t(15,17) Fusion	red/green	10	KBI-10302
ON PML/RARA t(15,17) Fusion	red/green	20	KBI-12302

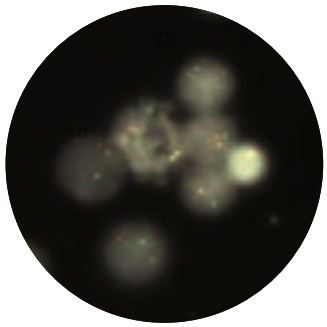
ON MLL (11q23) Break

The human chromosome band 11q23 is associated with a high number of recurrent chromosomal abnormalities including translocations, insertions, and deletions. It is involved in over 20% of acute leukemias. The MLL (Myeloid-Lymphoid Leukemia or Mixed-Lineage Leukemia) gene, named for its involvement in myeloid (usually monoblastic) and lymphoblastic leukemia, and less commonly in lymphoma is located in the 11q23 breakpoint region. Leukemias involving the MLL gene usually have a poor prognosis.

The MLL (11q23) break probe is optimized to detect translocations involving the MLL gene region at 11q23 in a dual-color split assay.

Cat.# KBI-10303 MLL (11q23) Break





MLL (11q23) Break probe hybridized to patient material showing a translocation at 11q23 (1RG1R1G).

Literature:

Kobayashi et al, 1993, Blood, 81: 3027-3022
Martinez-Climent et al, 1995, Leukemia, 9: 1299-1304.

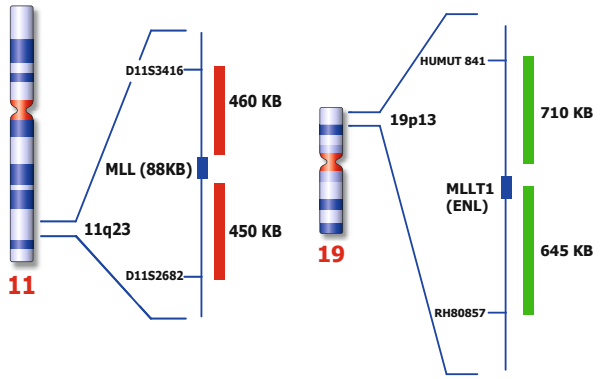
Ordering information	Color	Tests	Cat#
ON MLL (11q23) Break	red/green	10	KBI-10303

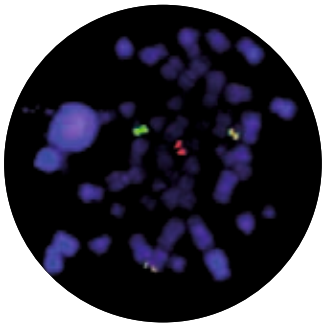
ON MLL/MLLT1 t(11;19) Fusion

One of the relatively frequently observed translocations (around 10 %) in human Acute Myeloid Leukemia (AML) and Acute Lymphoblastic Leukemia (ALL) involves the genes MLL and MLLT1 (aka ENL) at 11q23 and 19p13. The MLL/MLLT1 translocation results in the generation of fusion protein that retains the MLL N-terminus, including both an A-T hook domain and a region similar to mammalian DNA methyltransferase. There are several breakpoints within the MLLT1 gene described, without clear differences in clinicohematologic features. Patients with AML and the MLL/MLLT1 translocation carry a poor prognosis, but noninfant children with ALL and MLL/MLLT1 fusion may have a favorable prognosis.

The MLL/MLLT1 Fusion probe is optimized to detect translocations involving the MLL and MLLT1 gene regions at 11q23 and 19p13 in a dual-color, fusion assay on metaphase/interphase spreads, blood smears and bone marrow cells.

Cat# KBI-10307 MLL/MLLT1 t(11;19) Fusion





MLL/MLLT1 t(11;19) Fusion probe hybridized to patient material showing t(11;19) translocation (2RG1R1G).
Image kindly provided by Dr. Mohr, Dresden.

Literature:
Mitterbauer-Hohdanner G et al, 2004, Eur J Clin Invest, 34; 12-24.
Meyer C et al, 2009, Leukemia, 23; 1490-1499.
Fu JF et al, 2007, Am J Clin Pathol, 127; 24-30.

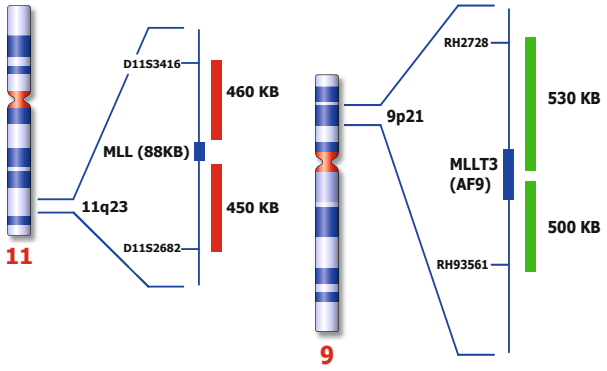
Ordering information	Color	Tests	Cat#
ON MLL/MLLT1 t(11;19) Fusion	red/green	10	KBI-10307

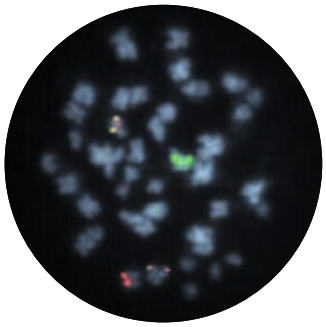
ON MLL/MLLT3 t(9;11) Fusion

Chromosomal rearrangements involving the mixed lineage leukemia (MLL) gene at 11q23 are frequently observed in adult and childhood acute leukemia and are, in general, associated with poor prognosis. However, children with Acute Myeloid Leukemia (AML) carrying the t(9;11) MLL/MLLT3 (aka AF9) translocation have been described to be more sensitive to chemotherapy than patients with other 11q23 rearrangements.

The MLL/MLLT3 Fusion probe is optimized to detect translocations involving the MLL and MLLT3 gene regions at 11q23 and 9p21 in a dual-color fusion assay on metaphase/interphase spreads, blood smears and bone marrow cells.

Cat# KBI-10308 MLL/MLLT3 t(9;11) Fusion





MLL/MLLT3 t(9;11) Fusion probe hybridized to patient material showing t(9;11) translocation (2RG1R1G).
Image kindly provided by Dr. Mohr, Dresden.

Literature:
Palle J et al, 2005, Br J Haematol, 129; 189-198.
Meyer C et al, 2009, Leukemia, 23; 1490-1499.
Cavazzini F et al, 2006, Haematologica, 91; 381-5.
Balgobind BV et al, 2009, Blood, 114; 2489-96.
Keefe JG et al, 2010, J Mol Diagn, 12; 441-452.

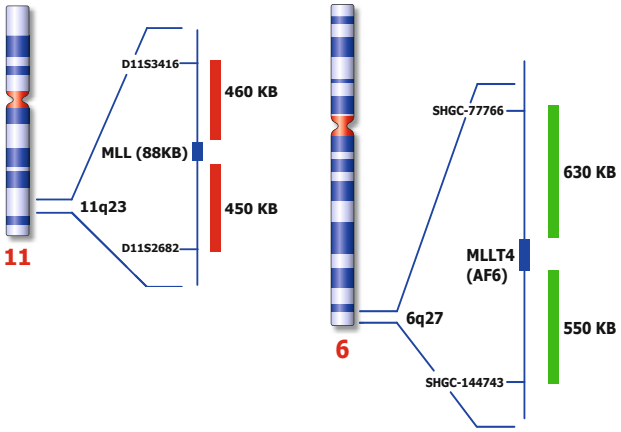
Ordering information	Color	Tests	Cat#
ON MLL/MLLT3 t(9;11) Fusion	red/green	10	KBI-10308

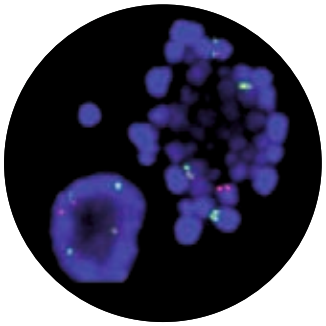
ON MLL/MLLT4 t(6;11) Fusion

One of the relatively frequently observed translocations in human Acute Myeloid Leukemia (AML) involves the genes MLL and MLLT4 (aka AF6) at 11q23 and 6q27. The MLL/MLLT4 translocation results in the generation of fusion protein that retains the MLL N-terminus, including both an A-T hook domain and a region similar to mammalian DNA methyltransferase. The breakpoint region of the MLLT4 gene is located within intron 1 and downstream of the initiation codon. In all age groups and all phenotypes of leukemia, the MLL/MLLT4 translocation carries a poor prognosis.

The MLL/MLLT4 t(6;11) Fusion probe is optimized to detect translocations involving the MLL and MLLT4 gene regions at 11q23 and 6q27 in a dual-color, fusion assay on metaphase/interphase spreads, blood smears and bone marrow cells.

Cat# KBI-10309 MLL/MLLT4 t(6;11) Fusion





MLL/MLLT4 t(6;11) Fusion probe hybridized to patient material showing 47,XX,t(6;11)(q27;q23),+der(6)t(6;11)(q27;q23).
Image kindly provided by Dr. Mohr, Dresden.

Literature:

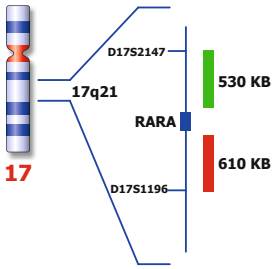
Mitterbauer-Hohdanner G et al, 2004, Eur J Clin Invest, 34; 12-24.
Meyer C et al, 2009, Leukemia, 23; 1490-1499.

Ordering information	*Color*	*Tests*	*Cat#*
ON MLL/MLLT4 t(6;11) Fusion	red/green	10	KBI-10309

ON RARA (17q21) Break

This break apart probe can detect the numerous types of recurrent rearrangement of the RARα (Retinoid acid receptor, alpha) gene with various gene partners (e.g., PML, NPM, MLL, FIP1L1, NuMA1, PLZF, amongst the others), leading to the formation of different reciprocal fusion proteins. The importance of retinoid metabolism in acute promyelocytic leukemia (APL) is highlighted by the numerous recent studies, but the different leukemogenic functions of the RARα fusion proteins in the neoplastic myeloid development still has to be defined, as well as the distinct clinical outcome of the patients with the variant forms of APL.

Cat.# KBI-10305 RARA (17q21) Break



RARA (17q21) Break probe hybridized to patient material showing a translocation at 17q21 (1RG1R1G).

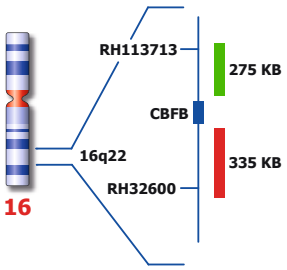
Ordering information	*Color*	*Tests*	*Cat#*
ON RARA (17q21) Break	red/green	10	KBI-10305

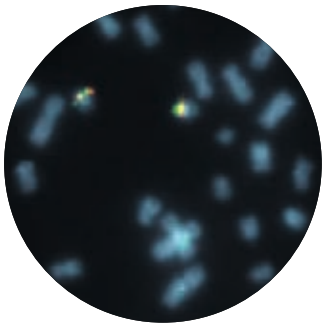
ON CBFB t(16;16); inv(16) Break

Inv(16)(p13;q22) and t(16;16)(p13;q22) are recurring chromosomal rearrangements in AML. In both the inversion and translocation, the critical genetic event is the fusion of the CBFB gene at 16q22 to the smooth muscle myosin heavy chain (MYH11) at 16p13. A deletion of between 150 and 350 kb centromeric to the p-arm inversion breakpoint cluster region can be observed in some patients containing the 5' portion of the myosin heavy chain (MYH11) gene.

The CBFB t(16;16) inv(16) break probe is optimized to detect the inversion of chromosome 16 involving the CBFB gene region at 16q22 in a dual-color, split assay.

Cat.# KBI-10304 CBFB t(16;16); inv(16) Break





CBFB t(16;16); inv(16) Break probe hybridized to a normal metaphase (2RG).

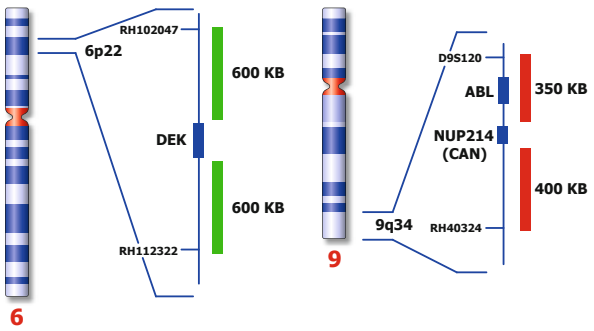
Literature:
Dauwerse et al, 1993, Hum.Mol.Genet., 2: 1527-1534.
Marlton et al, 1995, Blood, 85: 772-779.

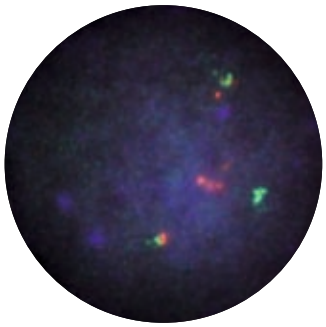
Ordering information	Color	Tests	Cat#
ON CBFB t(16;16); inv(16) Break	red/green	10	KBI-10304

ON DEK / NUP214 t(6;9) Fusion

The chromosomal translocation t(6;9) (p22;q34) is associated with a specific subtype of acute myeloid leukemia (AML) and constitutes 0.5% to 4% of all AML cases. The translocation results in a fusion between the DEK oncogene (6p22) and the nucleoporin 214 kDa (NUP214 at 9q34; previously known as CAN). The exact mechanism by which the fusion protein DEK-NUP214 contributes to leukemia development has not been identified. Patients with t(6;9) AML have a very poor prognosis. The currently available chemotherapy does not seem to improve overall survival. However, accurate diagnosis is crucial because these patients may benefit from early allogeneic stem cell transplant.
The DEK / NUP214 t(6;9) specific DNA Probe has been optimized to detect the reciprocal translocation t(6;9) in a dual-color, dual-fusion assay on metaphase/interphase spreads, blood smears and bone marrow cells.

Cat.# KBI-10306 DEK / NUP214 t(6;9) Fusion probe





DEK / NUP214 t(6;9) Fusion probe hybridized to patient material showing a t(6;9)(p22;q34) translocation (2RG1R1G).
Image kindly provided by Dr. Stevens-Kroef, UMC St. Radboud, Nijmegen.

Literature:
Von Lindern et al, 1992, Mol. Cell. Biol.,12; 1687-1697.
Ageberg et al, 2008, Gen. Chrom. Canc., 47; 276-287.
Chi et al, 2008, Arch. Pathol. Lab. Med.,132; 1835-1837.

Ordering information	Color	Tests	Cat#
ON DEK / NUP214 t(6;9) Fusion	red/green	10	KBI-10306

Acute Lymphoblastic Leukemia (ALL)

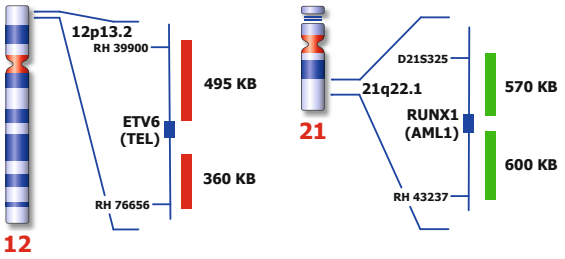
Acute lymphocytic leukemia, also called acute lymphoblastic leukemia, is a type of cancer that starts from white blood cells in the bone marrow. A number of recurring cytogenetic abnormalities are associated with distinct immunologic phenotypes of ALL and characteristic outcomes. The ETV6 (TEL) / RUNX1 (AML1) fusion arising from the translocation t(12;21)(p13;q22) has been associated with a good outcome; the BCR/ABL fusion of t(9;22)(q34;q11), rearrangements of the MLL gene (11q23), and abnormalities of the short arm of chromosomes 9 involving the tumor suppressor genes p16 (INK4A) have a poor prognosis.

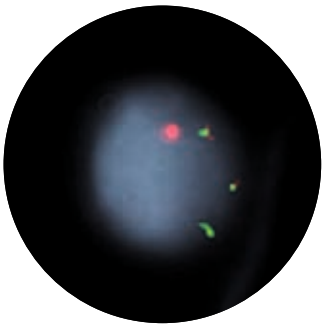
ON TEL/AML t(12;21) Fusion

The t(12;21), a cryptic translocation rarely observed by conventional cytogenetics, was first identified by fluorescence in situ hybridization (FISH). In ALL blasts, this translocation fuses the 5' part of the TEL (ETV6) gene with almost the entire AML1 (CBFA2) gene, producing the chimeric transcript ETV6-CBFA2. The t(12;21) (p13;q22) has also been identified as the most frequent chromosomal abnormality in childhood ALL, affecting 20% to 25% of B-lineage cases.

The TEL/AML t(12;21) specific DNA probe is optimized to detect the reciprocal translocation t(12;21) (p13;q22) in a dual-color, dual-fusion assay.

Cat.# KBI-10401 TEL/AML t(12;21) Fusion





TEL/AML t(12;21) Fusion probe hybridized to patient material showing t(12;21)translocation (2RG1R1G).
Material kindly provided by Dr. Balogh, Budapest.

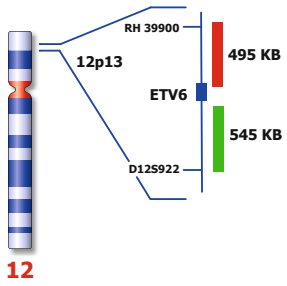
Literature:
Romana et al, 1995, Blood, 85: 3662-3670.

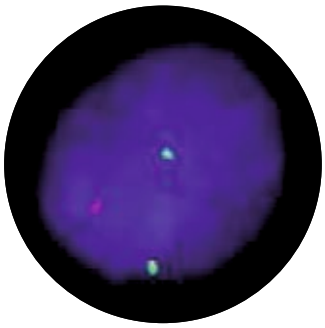
Ordering information	*Color*	*Tests*	*Cat#*
ON TEL/AML t(12;21) Fusion	red/green	10	KBI-10401

ON ETV6 (TEL) (12p13) Break

ETV6 (TEL) gene is the abbreviation for -ETS variant 6- gene. It encodes an ETS family factor which functions as a transcriptional repressor in hematopoiesis and in vascular development. The gene is located on chromosome 12p13, and is frequently rearranged in human leukemias of myeloid or lymphoid origins. Also systematic deletion of the normal ETV6 allele in patients with ETV6-AML1 fusions can be found.

Cat.# KBI-10403 ETV6 (TEL) (12p13) Break





ETV6 (TEL) (12p13) Break probe hybridized to patient material showing a translocation involving the ETV6 region at 12p13 (1RG1R1G). Image kindly provided by Magret Ratjen, Kiel.

Literature:
Golub et al, 1995, PNAS 92; 4917-4921.
Ford et al, 2001, Blood 98; 558-564.

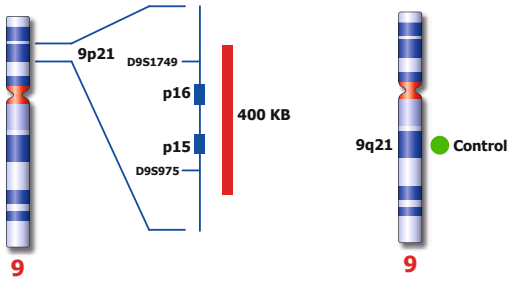
Ordering information	*Color*	*Tests*	*Cat#*
ON ETV6 (TEL) (12p13) Break	red/green	10	KBI-10403

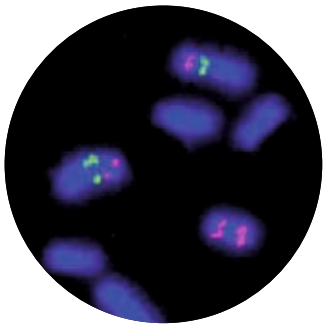
ON p16 (9p21) / 9q21

Hemizygous deletions and rearrangements of chromosome 9, band p21 are among the most frequent cytogenetic abnormalities detected in pediatric acute lymphoblastic leukemia (ALL). This deletion includes loss of the p16 (CDKN2A)/p15 (CDKN2B) genes, which are cell cycle kinase inhibitors and important in leukemogenesis.

The p16 (9p21) specific DNA probe is optimized to detect copy numbers of the p16 (INK4A) gene region at region 9p21. The 9q21 region probe is included to facilitate chromosome identification.

Cat.# KBI-10402 p16 (9p21) / 9q21





p16 (9p21) / 9q21 hybridized on patient material showing an isochromosome 9.
Image kindly provided by Dr. Wenzel, Basel.

Literature:
Dreyling et al, 1995, Blood, 86: 1931-1938.
Southgate et al, 1995, Br J Cancer, 72: 1214-1218.

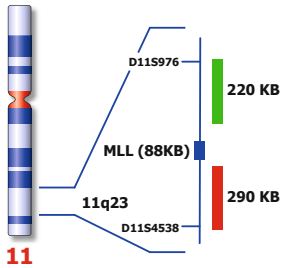
Ordering information	*Color*	*Tests*	*Cat#*
ON p16 (9p21) / 9q21	red/green	10	KBI-10402

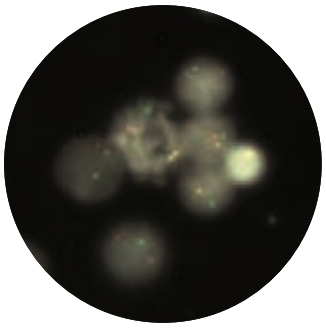
ON MLL (11q23) Break

The human chromosome band 11q23 is associated with a high number of recurrent chromosomal abnormalities including translocations, insertions, and deletions. It is involved in over 20% of acute leukemias. The MLL (Myeloid-Lymphoid Leukemia or Mixed-Lineage Leukemia) gene, named for its involvement in myeloid (usually monoblastic) and lymphoblastic leukemia, and less commonly in lymphoma is located in the 11q23 breakpoint region. Leukemias involving the MLL gene usually have a poor prognosis.

The MLL (11q23) break probe is optimized to detect translocations involving the MLL gene region at 11q23 in a dual-color split assay.

Cat.# KBI-10303 MLL (11q23) Break





MLL (11q23) Break probe hybridized to patient material showing a translocation at 11q23 (1RG1R1G).

Literature:

Kobayashi et al, 1993, Blood, 81: 3027-3022.
Martinez-Climent et al, 1995, Leukemia, 9: 1299-1304.

Ordering information	*Color*	*Tests*	*Cat#*
ON MLL (11q23) Break	red/green	10	KBI-10303

ON BCR/ABL t(9;22)

The t(9;22) BCR/ABL translocation is present in about 5% of pediatric and up to 50% of adult ALL cases, and is associated with poor prognosis.

Cat.# KBI-10005 ON BCR/ABL t(9;22) Fusion
Cat.# KBI-12005 ON BCR/ABL t(9;22) Fusion
Cat.# KBI-10006 ON BCR/ABL t(9;22) TC, D-Fusion
Cat.# KBI-10008 ON BCR/ABL t(9;22) DC, S-Fusion, ES
Cat.# KBI-10009 ON BCR/ABL t(9;22) DC, S-Fusion
Cat.# KBI-10013 ON Mm-BCR/ABL t(9;22), DC, S-Fusion, ES
See description under CML on page 11 and 12.

Ordering information	*Color*	*Tests*	*Cat#*
ON BCR/ABL t(9;22) Fusion	red/green	10	KBI-10005
ON BCR/ABL t(9;22) Fusion	red/green	20	KBI-12005
ON BCR/ABL t(9;22) TC, D-Fusion	red/green/blue	10	KBI-10006
ON BCR/ABL t(9;22) DC, S-Fusion, ES	red/green	10	KBI-10008
ON BCR/ABL t(9;22) DC, S-Fusion	red/green	10	KBI-10009
Mm-BCR/ABL t(9;22), DC, S-Fusion, ES	red/green	10	KBI-10013

Multiple Myeloma (MM)

The cytogenetic picture in multiple myeloma (MM) is highly complex, from which non-random numerical and structural chromosomal changes have been identified. Specifically, translocations involving the immunoglobulin heavy chain gene (IGH) at 14q32 and either monosomy or deletions of chromosome 13 have been observed in a significant number of patients. More recently several additional deletions or amplifications have been identified in MM which are currently investigated in large patient studies.

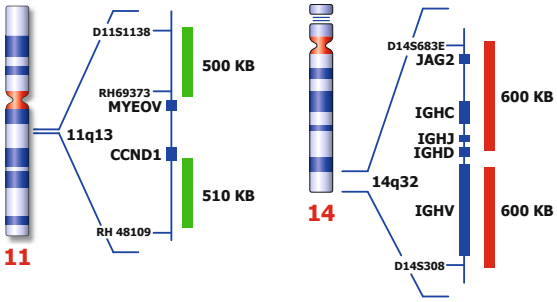
Note: Multiple Myeloma is a cancer of plasma cells. Analysis of such cells is hampered by their low frequency. Enrichment of plasma cells using CD138 is highly recommended.

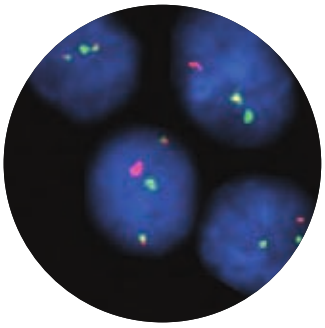
ON MYEOV/IGH t(11;14) Fusion

The most common chromosomal translocation in multiple myeloma (MM) is t(11;14), resulting in up-regulation of cyclin D1. In MM the breakpoints are scattered within a 360-kb region between CCND1 and MYEOV. This breakpoint is more proximal than the t(11;14) breakpoints observed in mantle cell lymphoma or other leukemias. Patients with MM who have t(11;14)(q13;q32) seem to have an aggressive clinical course.

The MYEOV/IGH t(11;14)(q13;q32) specific DNA probe is optimized to detect the reciprocal translocation t(11;14) in a dual-color, dual-fusion assay.

Cat.# KBI-10605 MYEOV/IGH t(11;14) Fusion





MYEOV/IGH t(11;14) Fusion probe hybridized to MM patient material showing t(11;14) translocation (2RG1R1G).
Image kindly provided by Prof. Jauch, Heidelberg.

Literature:
Janssen et al., 2000, Blood, 95: 2691-2698.
Fonseca et al, 2002, Blood, 99: 3735-3741.

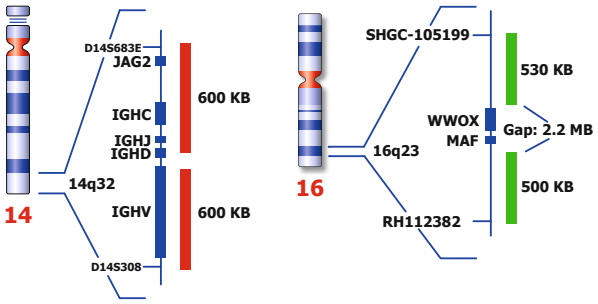
Ordering information	*Color*	*Tests*	*Cat#*
ON MYEOV/IGH t(11;14) Fusion	red/green	10	KBI-10605

ON MAF/IGH t(14;16) Fusion

Chromosome translocations involving the immunoglobulin heavy chain gene (IgH) on 14q32 are a fundamental event in the pathogenesis of many B-cell malignancies. It often is preceded by a stable pre-malignant tumor called Monoclonal Gammopathy of Undetermined Significance (MGUS), which can sporadically progress to Multiple Myeloma (MM). One of the recurrent primary rearrangements involving the immunoglobulin heavy chain (IgH) locus on chromosome 14q32 identified in MGUS and MM tumors is the MAF/IgH t(14;16) translocation. Following MGUS appearance, the pathogenesis of multiple myeloma (MM) is thought to involve at least two pathways, which generate hyperdiploid (HRD) or nonhyperdiploid (NHRD) tumors, respectively.

The MAF/IGH is mainly present in NHRD tumors, providing important information on MM patient sub-types. Since these translocations are caused by aberrant IgH switch recombination, and possibly by aberrant somatic hypermutation in germinal center B cells, they provide information of an early and perhaps initiating event of transformation.

Cat.# KBI-10610 MAF/IGH t(14;16) Fusion



MAF/IGH t(14;16) Fusion probe hybridized to patient material showing a deletion of the MAF gene region at 16q23 (2R1G).

Literature:
Chesi et at, 1998, Blood 91; 4457-4463.
Sawyer et al, 1998, Blood 92; 4269-4278.

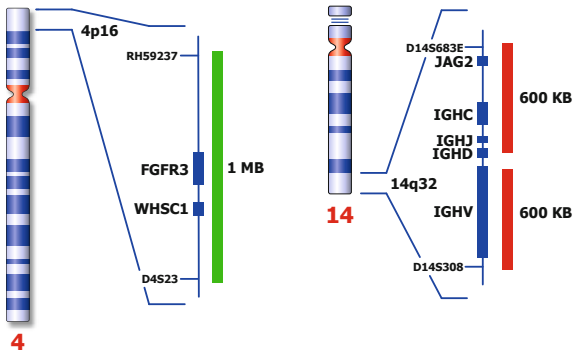
Ordering information	*Color*	*Tests*	*Cat#*
ON MAF/IGH t(14;16) Fusion	red/green	10	KBI-10610

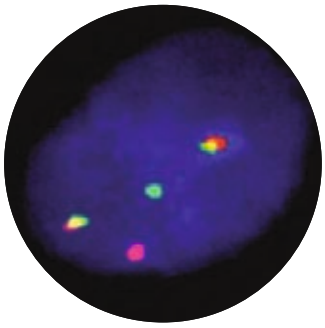
ON FGFR3/IGH t(4;14) Fusion

The t(4;14) translocation is undetectable by conventional cytogenetics. The breakpoints on chromosome 4 occur within an approximately 113-kb region located in small part of a conserved gene cluster including the transforming acidic coiled-coil protein 3 (TACC3), fibroblast growth factor receptor 3 (FGFR3), and multiple myeloma SET domain-containing protein (MMSET). The translocation is indicative for poor survival and poor response to chemotherapy.

The FGFR3/IGH t(4;14)(p16;q32) specific DNA probe is optimized to detect the reciprocal translocation t(4;14) in a dual-color, dual-fusion assay.

Cat.# KBI-10602 FGFR3/IGH t(4;14) Fusion





FGFR3/IGH t(4;14) Fusion probe hybridized to MM patient material showing t(4;14) translocation (2RG1R1G).
Image kindly provided by Prof. Jauch, Heidelberg.

Literature:
Chesi et al, 1997, Nat Genet, 16: 260-264.
Finelli et al, 1999, Blood, 94: 724-732.

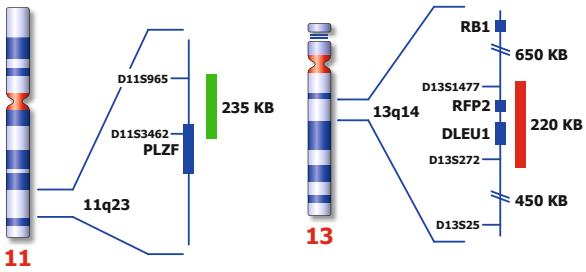
Ordering information	Color	Tests	Cat#
ON FGFR3/IGH t(4;14) Fusion	red/green	10	KBI-10602

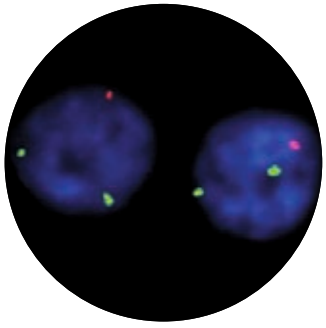
ON MM 11q23 / DLEU (13q14)

Hybridization results delineated 11q23 and 11q25 as the most frequently gained regions in MM, which supports a relevant pathogenetic role of genes in this region. Deletions of 13q14 are frequently detected by interphase FISH in patients with newly diagnosed MM, correlate with increased proliferative activity, and represent an independent adverse prognostic feature in MM.

The 11q23 specific DNA probe is optimized to detect copy numbers at 11q23. The DLEU (13q14) specific DNA region is optimized to detect copy numbers of the DLEU gene region at 13q14.

Cat.# KBI-10502 MM 11q23 / 13q14





MM 11q23 / DLEU 13q14 probe hybridized to MM patient material showing a 13q14 deletion (1R2G).
Image kindly provided by Prof. Jauch, Heidelberg.

Literature:
Gonzalez et al, 2004, Haematologica, 89: 1213-1218.
Cremer et al, 2005, Genes Chrom Cancer, 44: 194-203.

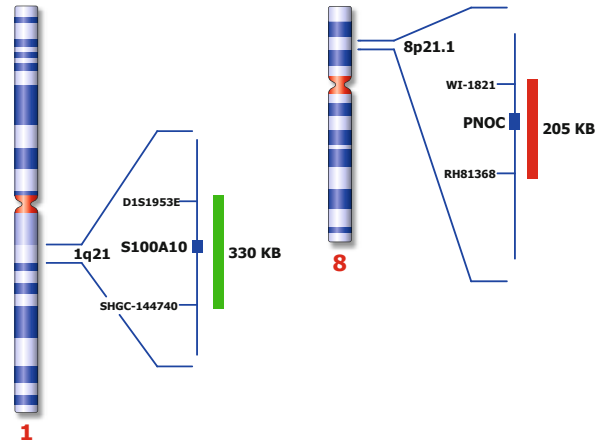
Ordering information	Color	Tests	Cat#
ON MM 11q23 / DLEU (13q14)	red/green	10	KBI-10502

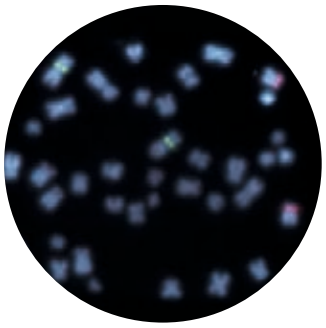
ON MM 1q21 / 8p21

Amplifications of 1q21 are concurrent with dysregulated expression of c-MAF, MMSET/FGFR3, or Del13 and represent an independent unfavorable prognostic factor. Allelic losses of the chromosome 8p21-22 have been reported as a frequent event in several cancers.

The 1q21 specific DNA probe is optimized to detect copy numbers at 1q21. The 8p21 specific DNA region is optimized to detect copy numbers at 8p21.

Cat.# KBI-10503 MM 1q21 / 8p21





MM 1q21 / 8p21 hybridized to a normal metaphase (2R2G).

Literature:

Shaughnessy J., 2005, Hematology, 10 suppl 1: 117-126.
Cremer et al, 2005, Genes Chrom Cancer, 44: 194-203.

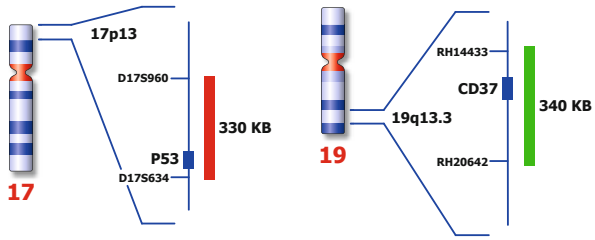
Ordering information	*Color*	*Tests*	*Cat#*
ON MM 1q21 / 8p21	red/green	10	KBI-10503

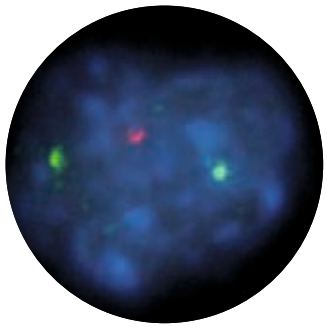
ON MM 19q13 / p53 (17p13)

P53 gene deletion, which can be identified by interphase FISH in almost a third of patients with newly diagnosed MM, is a novel prognostic factor predicting for short survival of MM patients treated with conventional-dose chemotherapy. Amplification of 19q13 has been reported in a variety of cancer.

The 19q13 specific DNA probe is optimized to detect copy numbers at 19q13. The p53 (17p13) specific DNA region is optimized to detect copy numbers of the p53 gene region at 17p13.

Cat.# KBI-10509 MM 19q13 / p53 (17p13)





MM 19q13 / p53 (17p13) hybridized to patient material showing a p53 (17p13) deletion (1R2G).
Image kindly provided by Prof. Jauch, Heidelberg.

Literature:

Drach et al, 1998, Blood, 92: 802-809.
Cremer et al, 2005, Genes Chrom Cancer, 44: 194-203.

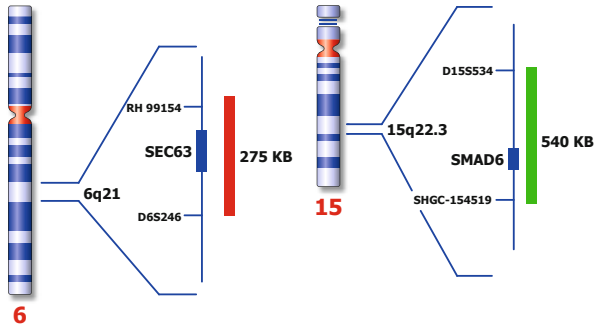
Ordering information	*Color*	*Tests*	*Cat#*
ON MM 19q13 / p53 (17p13)	red/green	10	KBI-10509

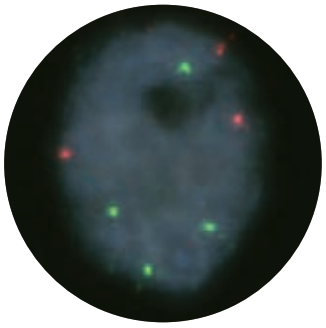
ON MM 15q22 / 6q21

Chromosome 6q amplifications encompassing 6q21-22 have been observed in MM including the same region as in CLL. Amplification including band 15q22 has been reported in MM.

The 15q22 specific DNA probe is optimized to detect copy numbers at 15q22. The 6q21 specific DNA region is optimized to detect copy numbers at 6q21.

Cat.# KBI-10504 MM 15q22 / 6q21





MM 15q22 / 6q21 hybridized to MM patient material with gain of both critical regions 6q21 and 15q22.
Image kindly provided by Prof. Jauch, Heidelberg.

Literature:
Cremer et al, 2005,
Genes Chrom Cancer, 44: 194-203.

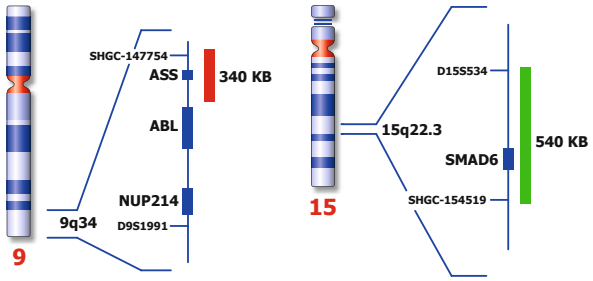
Ordering information	Color	Tests	Cat#
ON MM 15q22 / 6q21	red/green	10	KBI-10504

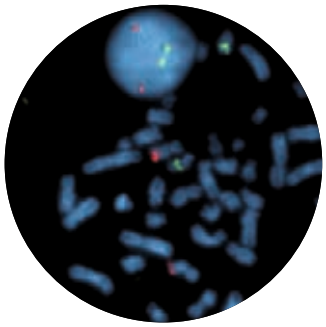
ON MM 15q22 / 9q34

The hyperdiploid subtype in MM is defined by presence of multiple trisomic chromosomes. Combination of the chromosome 9q34 and 15q22 specific regions are important regions to detect the hyperdiploid subtype in MM which is usually associated with a low frequency of IGH translocations.

The 15q22 and 9q34 probe is designed as a dual-color assay to detect amplifications at 15q22 and 9q34.

Cat.# KBI-10508 MM 15q22 / 9q34





MM 15q22 / 9q34 hybridized to a normal interphase/ metaphase (2R2G).

Literature:
Cremer et al, 2005,
Genes Chrom Cancer, 44: 194-203.

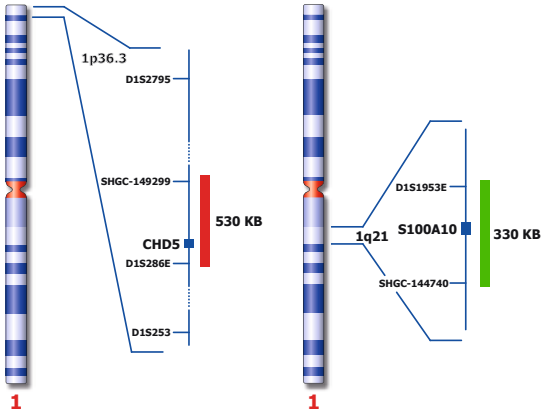
Ordering information	Color	Tests	Cat#
ON MM 15q22 / 9q34	red/green	10	KBI-10508

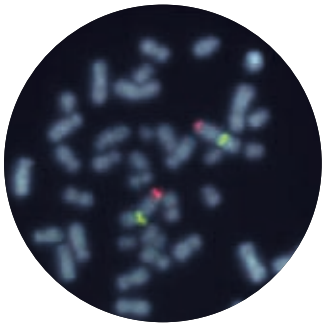
ON MM 1q21 / SRD (1p36)

Frequent loss of heterozygosity (LOH) on the short arm of chromosome 1 (1p) has been reported in a series of human malignancies.

The 1q21 specific DNA probe is optimized to detect copy numbers at 1q21. The SRD 1p36 specific DNA Probe is optimized to detect copy numbers of 1p at region 1p36 containing the markers D1S2795 and D1S253.

Cat.# KBI-10507 MM 1q21 / SRD (1p36)





MM 1q21 / SRD (1p36) hybridized to a normal metaphase (2R2G).

Literature:

Cremer et al, 2005, Genes Chrom Cancer, 44: 194-203.
Shaughnessy J., 2005, Hematology, 10 suppl 1: 117-126.

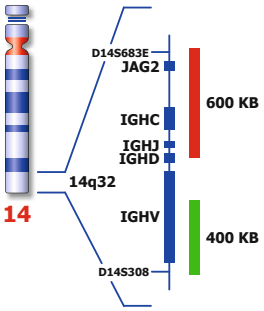
Ordering information	Color	Tests	Cat#
ON 1q21 / SRD (1p36)	red/green	10	KBI-10507

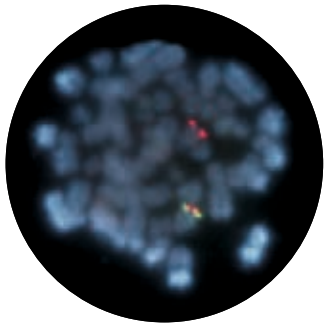
ON IGH (14q32) Break

Multiple myeloma is characterized by complex rearrangements involving the IgH gene, particularly at the constant locus. The IgH rearrangement provides a useful marker of clonality in B-cell malignancies and amplification of this rearrangement is the method of choice to monitor the residual tumor cells in multiple myeloma.

The IGH (14q32) break probe is optimized to detect translocations involving the IGH gene region at 14q32 in a dual-color, split assay.

Cat.# KBI-10601 IGH (14q32) Break





IGH (14q32) Break probe hybridized to patient material showing a partial deletion of 14q32 (1RG1R).

Literature:

Taniwaki et al, 1994, Blood, 83: 2962-1969.
Gozetti et al, 2002, Cancer Research, 62: 5523-5527.

Ordering information	Color	Tests	Cat#
ON IGH (14q32) Break	red/green	10	KBI-10601

Lymphoma

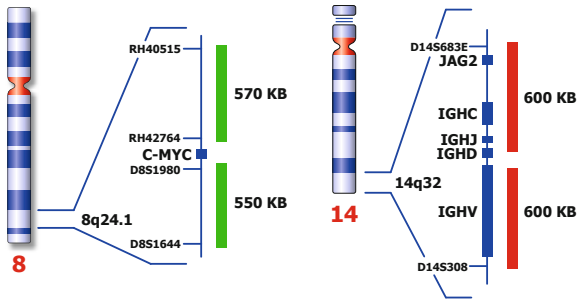
Lymphoma is a type of cancer that originates in lymphocytes. Following WHO classification there are three large groups: B cell lymphomas, T cell and natural killer cell tumors, and Hodgkin lymphoma. The IGH gene locus at chromosome band 14q32 is very frequently involved in B-cell lymphoma.

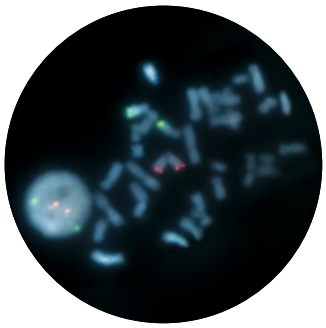
ON MYC/IGH t(8;14) Fusion

The translocation t(8;14)(q24;q32) is the characteristic chromosomal aberration of Burkitt's-type of lymphomas. This translocation fuses the C-MYC gene at 8q24 next to the IGH locus at 14q32, resulting in overexpression of the transcription factor C-MYC. Detection of the t(8;14) is aimed to help in the diagnostic process of patients with high-grade B-cell lymphomas because treatment strategies differ between Burkitt and other high-grade lymphomas.

The MYC/IGH t(8;14)(q24;q32) specific DNA probe is optimized to detect the reciprocal translocation t(8;14) in a dual-color, dual-fusion assay.

Cat.# KBI-10603 MYC/IGH t(8;14) Fusion





MYC/IGH t(8;14) Fusion probe hybridized to a normal interphase/ metaphase (2R2G).

Literature:

Veronese et al, 1995, Blood, 85: 2132-2138.
Siebert et al, 1998, Blood, 91: 984-990.

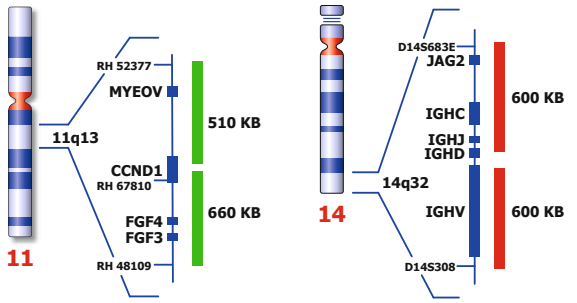
Ordering information	*Color*	*Tests*	*Cat#*
ON MYC/IGH t(8;14) Fusion	red/green	10	KBI-10603

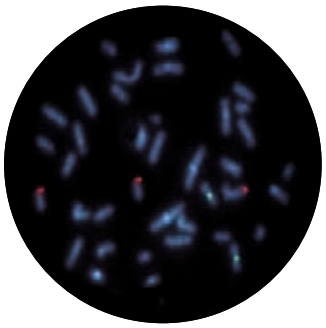
ON BCL1/IGH t(11;14) Fusion

Mantle cell lymphoma is a subtype of non-Hodgkin lymphoma characterized by poor prognosis. Cytogenetically t(11;14) is associated with 75% of mantle cells lymphomas. The translocation breakpoints are scattered within the 120 kb BCL1 region adjacent to CCND1. The translocation leads to overexpression of cyclin D1 due to juxtaposition of the Ig heavy chain gene enhancer on 14q32 to the cyclin D1 gene on 11q13.

The BCL1/IGH t(11;14)(q13;q32) specific DNA probe is optimized to detect the reciprocal translocation t(11;14) in a dual-color, dual-fusion assay.

Cat.# KBI-10604 BCL1/IGH t(11;14) Fusion





BCL1/IGH t(11;14) Fusion probe hybridized to a normal interphase/ metaphase (2R2G).

Literature:

Vaandrager et al, 1996, Blood, 88: 1177-1182.

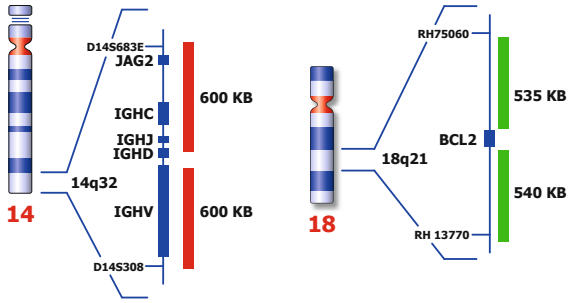
Ordering information	Color	Tests	Cat#
ON BCL1/IGH t(11;14) Fusion	red/green	10	KBI-10604

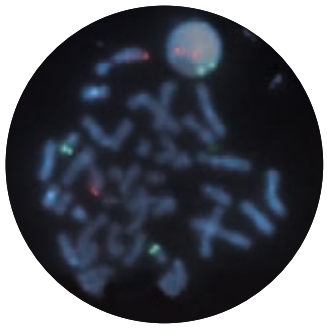
ON BCL2/IGH t(14;18) Fusion

The t(14;18) chromosomal translocation that results in the juxtaposition of the BCL2 proto-oncogene with the heavy chain JH locus. It a common cytogenetic abnormality in human lymphoma and is observed in about 85% of follicular lymphoma (FL) and up to one-third of diffuse lymphomas (DL). Two breakpoint region clusters (brc) have been identified: a major breakpoint region (mbr) within the 3' untranslated region of the BCL2 proto-oncogene accounting for approximately 60% of the cases and a minor cluster region (mcr) 30 kb 3' of BCL2 accounting for approximately 25% of the breakpoints.

The BCL2/IGH t(14;18)(q21;q32) specific DNA probe is optimized to detect the reciprocal translocation t(18;14), involving either of the two brc in the BCL2 gene in a dual-color, dual-fusion assay. KREATECH has optimized this probe for the specific use on cell material (KBI-10606), or for the use on tissue (KBI-10755).

Cat.# KBI-10606 BCL2/IGH t(14;18) Fusion





BCL2/IGH t(14;18) probe hybridized to a normal interphase/ metaphase (2R2G).

Literature:

Poetsch et al, 1996, J Clin Oncol, 14: 963-969.
Vaandrager et al, 2000, Genes Chrom Cancer, 27: 85-94.

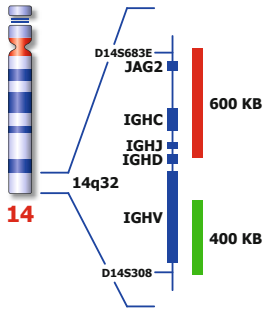
Ordering information	Color	Tests	Cat#
ON BCL2/IGH t(14;18) Fusion	red/green	10	KBI-10606

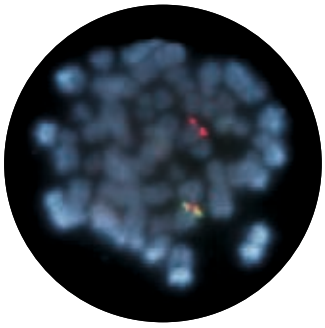
ON IGH (14q32) Break

Chromosomal rearrangements involving the immunoglobulin heavy chain gene (IGH) at 14q32 are observed in 50% of patients with B-cell non-Hodgkin's lymphoma (NHL) and many other types of Lymphomas. More than 50 translocation partners with IGH have been described. In particular t(8;14), is associated with Burkitt's lymphoma, t(11;14) is associated with Mantle cell lymphoma, t(14;18) is observed in a high proportion of follicular lymphomas and t(3;14) is associated with Diffuse Large B-Cell Lymphoma.

The IGH (14q32) break probe is optimized to detect translocations involving the IGH gene region at 14q32 in a dual-color, split assay. Kreatech has developed this probe for the specific use on cell material (KBI-10601), or for the use on tissue (KBI-10729).

Cat.# KBI-10601 IGH (14q32) Break





IGH (14q32) Break probe hybridized to patient material showing a partial deletion of 14q32 (1RG1R).

Literature:

Taniwaki et al, 1994, Blood, 83: 2962-1969.
Gozetti et al, 2002, Cancer Research, 62: 5523-5527.

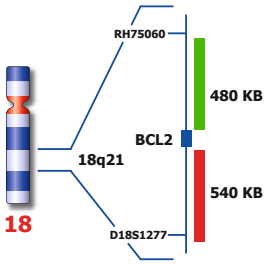
Ordering information	Color	Tests	Cat#
ON IGH (14q32) Break	red/green	10	KBI-10601

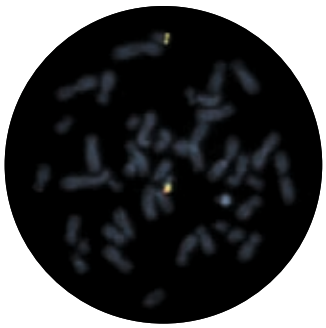
ON BCL2 (18q21) Break

Follicular lymphoma is a mature B-cell lymphoma characterized by the presence of the t(14;18) translocation that juxtaposes the BCL2 locus on chromosome 18q21 to the immunoglobulin H (IGH) locus on chromosome 14q32, resulting in the overexpression of the anti-apoptotic protein BCL2. Next to IGH, other translocation partners to BCL2 are also known (e.g. IGK at 2p11.2 and IGL at 22q11). A break or split assay is therefore best suited to detect rearrangements of the BCL2 gene region at 18q21.

The BCL2 (18q21) Break probe is optimized to detect translocations involving the BCL2 gene region at 18q21 in a dual-color, split assay on metaphase/interphase spreads, bloodsmears and bone marrow cells.

Cat# KBI-10612 BCL2 (18q21) Break





BCL2 (18q21) Break probe hybridized to a normal metaphase.

Literature:

Taniwaki M et al, 1995, Blood, 86; 1481-1486.
Poetsch M et al, 1996, J Clin Oncol, 14; 963- 969.
Einerson R et al, 2005, Am J Clin Pathol, 124; 421-429.

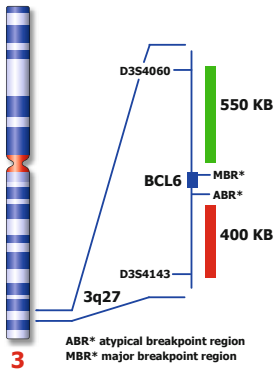
Ordering information	Color	Tests	Cat#
ON BCL2 (18q21) Break	red/green	10	KBI-10612

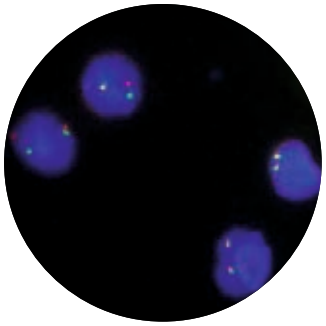
ON BCL6 (3q27) Break

Chromosomal translocations involving band 3q27 with various different partner chromosomes represent a recurrent cytogenetic abnormality in B-cell non-Hodgkin's lymphoma. A FISH strategy using two differently labeled flanking BCL6 probes provides a robust, sensitive, and reproducible method for the detection of common and uncommon abnormalities of BCL6 gene in interphase nuclei. Kreatech has developed this probe for the specific use on cell material (KBI-10607), or for the use on tissue (KBI-10730).

Two different breakpoint regions have been identified; the major breakpoint region **(MBR)** is located within the 5' noncoding region of the BCL6 proto-oncogene, while the atypical breakpoint region **(ABR)** is located approximately 200 kb distal to the BCL6 gene. The BCL6 (3q27) Break probe is designed in a way to flank both possible breakpoints, thereby providing clear split signals in either case.

Cat.# KBI-10607 BCL6 (3q27)





BCL6 (3q27) Break probe hybridized to patient material (1RG1R1G).
Image kindly provided by Prof. Siebert, Kiel.

Literature:

Butler et al, 2002, Cancer Res, 62; 4089-4094.
Sanchez-Izquierdo, 2001, Leukemia, 15; 1475-1484.

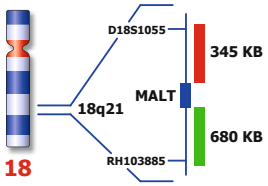
Ordering information	*Color*	*Tests*	*Cat#*
ON BCL6 (3q27) Break	red/green	10	KBI-10607

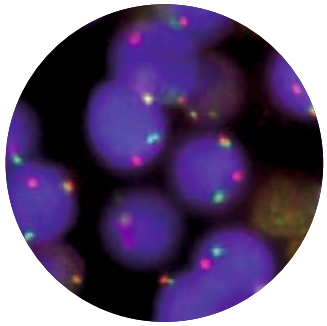
ON MALT (18q21) Break

Low grade malignant lymphomas arising from mucosa associated lymphoid tissue (MALT) represent a distinct clinicopathological entity. The three major translocations seen in MALT lymphomas are t(11;18)(q21;q21)/API2-MALT1, t(14;18)(q32;q21)/IGH-MALT1 and t(1;14)(p22;q32)/IGH-BCL10. A break or split probe for MALT (18q21) is best used to analyze translocation of the MALT gene on formalin fixed paraffin embedded tissue for routine clinical diagnosis.

Kreatech has optimized this probe for the specific use on cell material (KBI-10608), or for the use on tissue (KBI-10731).

Cat.# KBI-10608 MALT (18q21) Break





MALT (18q21) Break probe hybridized to patient material showing a translocation at 18q21 (1RG1RG).

Literature:

Morgan et al, 1999, Cancer Res, 59; 6205-6213.
Dierlamm et al, 2000, Blood, 96; 2215-2218.

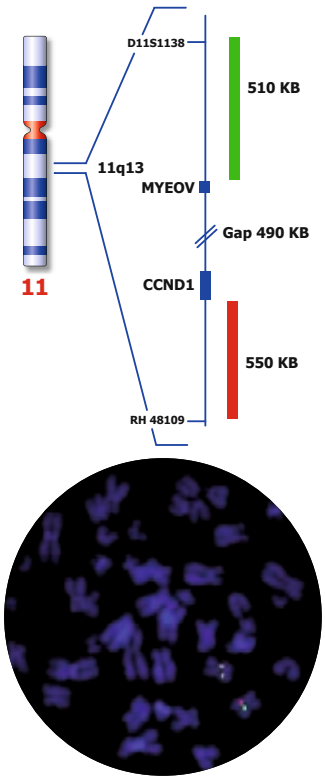
Ordering information	*Color*	*Tests*	*Cat#*
ON MALT (18q21) Break	red/green	10	KBI-10608

ON CCND1 (BCL1;11q13) Break

Besides the important functions in cellular growth, metabolism, and cellular differentiation, CCND1 (also known as Cyclin D1 or BCL1) can also function as a proto-oncogene, often dysregulated after re-arrangement by translocation. In fact, it can juxtapose into many different gene locus to drive tumorigenic effects. To date, the gene has been found to be rearranged in leukemias, in multiple myelomas (MM), and in some cases of benign parathyroid tumors. More specifically, the chromosomal translocation t(11;14)(q13:q32), involving rearrangement of the CCND1 locus, has been reported to be associated with human lymphoid neoplasia affecting mantle cell lymphomas (MCL).

The rearrangement has been documented in 40-70% of cases of mantle cell lymphoma, whereas it only rarely occurs in other B cell lymphomas. In multiple myeloma, the same translocation t(11;14)(q13:q32) is the most common, with a reported frequency of 15% to 20% of the cases. For this reason, the CCND1 break apart probe KBI-10609 can be considered a very useful tool for routine diagnosis in MCL and Multiple myeloma, to be used in association to the related probes KBI-10604 and KBI-10605 probes that can detect more specifically the translocation t(11;14) in Mantle Cell Lymphoma (KBI-10604) and Multiple Myeloma (KBI-10605).

Cat.# KBI-10609 CCND1 (BCL1; 11q13) Break



CCND1 (BCL1; 11q13) Break probe hybridized to a normal metaphase (2R2G).

Literature:

Vaandrager et al, 1996, Blood, 88 (4); 1177-1182.
Vaandrager et al, 1997, Blood, 89; 349-350.

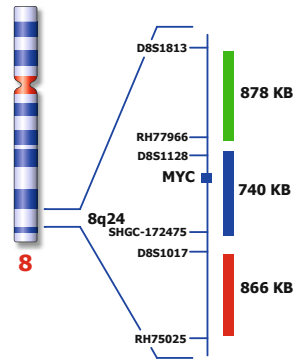
Ordering information	*Color*	*Tests*	*Cat#*
ON CCND1 (BCL1;11q13) Break	red/green	10	KBI-10609

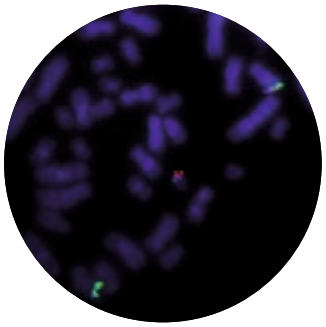
ON MYC (8q24) Break, TC

Rearrangements of the protooncogene C-myc (or MYC) have been consistently found in tumor cells of patients suffering from Burkitt's lymphoma. In cases with the common t(8;14) chromosomal translocation, the c-myc gene is translocated to chromosome 14 and rearranged with the immunoglobulin heavychain genes; the breakpoint occurs 5' to the c-myc gene and may disrupt the gene itself separating part of the first untranslated exon from the remaining two coding exons. In Burkitt's lymphoma showing the variant t(2;8) or t(8;22) translocations, the genes coding for the k and l mmunoglobulin light chain are translocated to chromosome 8. The rearrangement takes place 3' to the c-myc gene.

The MYC (8q24) break-apart probe is optimized to detect rearrangements involving the 8q24 locus in a triple-color, split assay on metaphase/interphase spreads, blood smears and bone marrow cells.

Cat.# KBI-10611 MYC (8q24) Break, TC





MYC (8q24) Break probe hybridized to patient material showing a 8q24 proximal break (1GBR1G1BR).
Image kindly provided by Prof. Siebert, Kiel.

Literature:
Fabris et al, 2003, Genes Chromosomes Cancer 37 ; 261-269.
Hummel et al., 2006, N Engl J Med 354 ;2419-30.

Ordering information	*Color*	*Tests*	*Cat#*
ON MYC (8q24) Break, TC	red/green	10	KBI-10611

ON FGFR3/IGH t(4;14) Fusion

Cat.# KBI-10602 FGFR3/IGH t(4;14) Fusion
See description under Multiple Myeloma on page 38.

Ordering information	*Color*	*Tests*	*Cat#*
ON FGFR3/IGH t(4;14) Fusion	red/green	10	KBI-10602

ON MYEOV/IGH t(11;14) Fusion

Cat.# KBI-10605 MYEOV/IGH t(11;14) Fusion
See description under Multiple Myeloma on page 36.

Ordering information	*Color*	*Tests*	*Cat#*
ON MYEOV/IGH t(11;14) Fusion	red/green	10	KBI-10605

ONCOLOGY - SOLID TUMOR DNA PROBES

In solid tumors significantly high levels of chromosome abnormalities have been detected, but distinction between significant (drivers) and irrelevant events (passengers) has been a major challenge. Consequently, the application of cytogenetic technology as diagnostic, prognostic, or therapeutic tools for these malignancies has remained largely underappreciated. The emergence of FISH is particularly useful for solid malignancies, and the spectrum of their application is rapidly expanding to improve efficiency and sensitivity in cancer diagnosis, prognosis, and therapy selection, alone or with other diagnostic methods. The REPEAT-FREE™ POSEIDON™ Solid Tumor DNA Probes are direct labeled, Ready-to-Use in hybridization buffer. The solid tumor probes are designed for the use on Formalin Fixed Paraffin Embedded (FFPE) tissue samples.

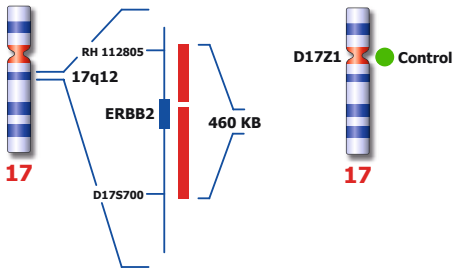
Table of Contents

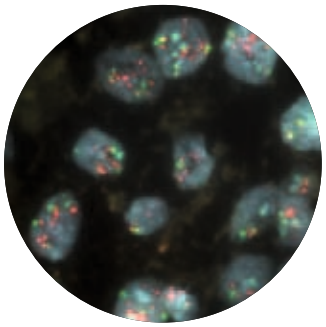
Breast Cancer

ON ERBB2, Her2/Neu (17q12) / SE 17

The Her2/Neu gene encodes a receptor tyrosine kinase involved in growth factor signaling. Overexpression of this gene is seen in about 20% of invasive breast cancers and is without proper treatment associated with poor survival. Her2 gene amplification is a permanent genetic change that results in this continuous overexpression of Her2. Trastuzumab (commonly known as Herceptin) has been developed to be effective against Her2-positive breast cancer. Her2/Neu amplification is also observed in a variety of other tumors, such as prostate, lung, colon and ovary carcinoma. The Her2/Neu (17q12) specific DNA probe is optimized to detect copy numbers of the Her2/Neu (ERBB2) gene region at region 17q12. The chromosome 17 satellite enumeration probe (SE 17) at D17Z1 is included to facilitate chromosome identification/enumeration.

Cat.# KBI-10701 ERBB2, Her2/Neu (17q12) / SE 17





ERBB2, Her2/Neu (17q12) / SE 17 probe hybridized to breast tumor tissue showing amplification of Her2/Neu (ERBB2)/ SE 17.

Literature:

Pauletti et al, 1996, Oncogene, 13: 63-72.
Xing, et al, 1996, Breast Cancer Res Treat, 39: 203-212.

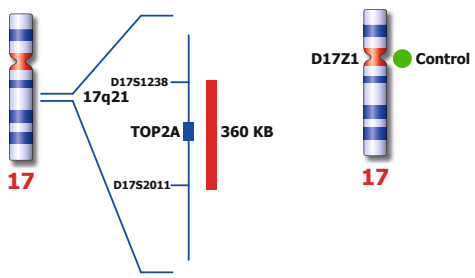
Ordering information	*Color*	*Tests*	*Cat#*
ON ERBB2, Her2/Neu (17q12) / SE 17	red/green	10	KBI-10701
ON ERBB2, Her2/Neu (17q12) / SE 17	red/green	50	KBI-14701

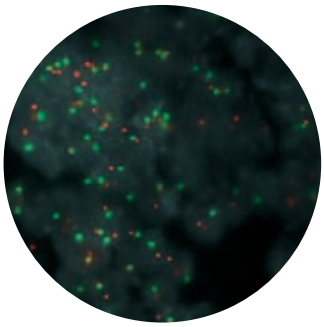
ON TOP2A (17q21) / SE 17

The Topoisomerase2A enzyme, which is vital for the cell because of its role in cell replication and repair, catalyzes the relaxation of supercoiled DNA molecules to create a reversible double-strand DNA break. This enzyme is also the target of a number of cytotoxic agents, namely TOP2A inhibitors (anthracyclines, etoposide, teniposide).

The dual-color probe is optimized to detect amplifications (copy numbers) or deletions of the TOP2A gene region at the 17q21. The chromosome 17 satellite enumeration probe (SE 17) at D17Z1 is included to facilitate chromosome identification.

Cat.# KBI-10724 TOP2A (17q21) / SE 17





TOP2A (17q21) / SE 17 probe hybridized to breast tissue (2R2G).

Literature:

Järvinen et al, 1999, Genes, Chromosomes and Cancer 26; 142-150.
Järvinen et al, 2000, Am. J. Pathology 156; 639-647.

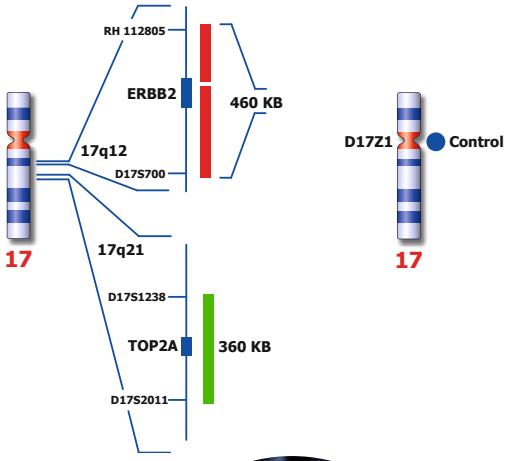
Ordering information	*Color*	*Tests*	*Cat#*
ON TOP2A (17q21) / SE 17	red/green	10	KBI-10724

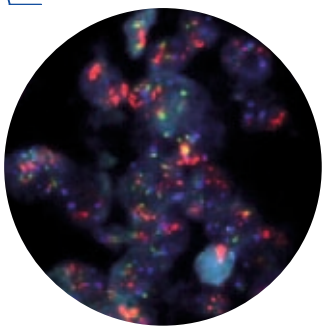
ON TOP2A (17q21) / Her2 (17q12) / SE 17 Triple-Color Probe

The presence of both TOP2A amplification and deletion in advanced cancer are associated with decreased survival, and occur frequently and concurrently with Her2 gene amplification.

The TOP2A (17q21)/ Her2 (17q12)/ SE 17 probe is designed as a triple-color assay to detect amplification at 17q12 as well as amplifications or deletions at 17q21. The chromosome 17 satellite enumeration probe (SE 17) at D17Z1 in blue is included to facilitate chromosome identification/enumeration.

Cat.# KBI-10735 TOP2A (17q21) / Her2 (17q12) / SE 17





TOP2A (17q21)/ Her2(17q12) / SE 17 TC probe hybridized to breast tumor tissue showing amplification of TOP2A/Her2.

Literature:
Järvinen et al, 1999, Genes, Chromosomes and Cancer 26; 142-150.
Järvinen et al, 2000, Am. J. Pathology 156; 639-647.

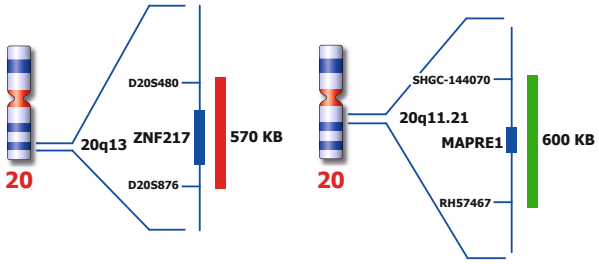
Ordering information	Color	Tests	Cat#
ON TOP2A (17q21) / Her 2 / SE 17	red/green	10	KBI-10735

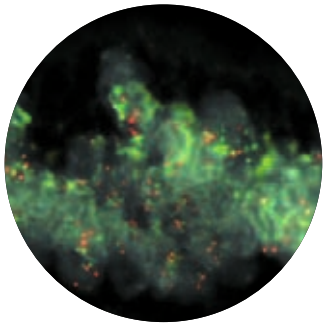
ON ZNF217 (20q13) / 20q11

Zinc-finger protein 217 (ZNF217) is a Kruppel-like zinc-finger protein located at 20q13.2, within a region of recurrent maximal amplification in a variety of tumor types, and especially breast cancer cell lines and primary breast tumors. Copy number gains at 20q13 are also found in more than 25% of cancers of the ovary, colon, head and neck, brain, and pancreas, often in association with aggressive tumor behavior. ZNF217 is considered a strong candidate oncogene that may have profound effects on cancer progression, which is transcribed in multiple normal tissues, and overexpressed in almost all cell lines and tumors in which it is amplified.

The ZNF217 (20q13) specific DNA probe is optimized to detect copy numbers of 20q at 20q13. The 20q11 probe is included to facilitate chromosome identification.

Cat.# KBI-10733 ZNF217 (20q13) / 20q11





ZNF217 (20q13) / 20q11 probe hybridized to tissue (2R2G).

Literature:
Tanner M et al, 2000, Clin Cancer Res, 6; 1833-1839.
Ginestier C et al, 2006, Clin Cancer Res, 12; 4533-4544.

Ordering information	Color	Tests	Cat#
ON ZNF217 (20q13) / 20q11	red/green	10	KBI-10733

ON FGFR1 (8p12) Break

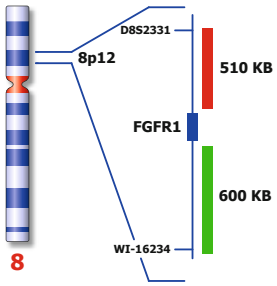
Translocations affecting the chromosomal locus FGFR1 (8p12) are hallmarks of an atypical stem cell myeloproliferative disorder. These events disrupt the fibroblast growth factor receptor 1 (FGFR1) gene and fuse the FGFR1 C-terminal catalytic domain with unrelated proteins.

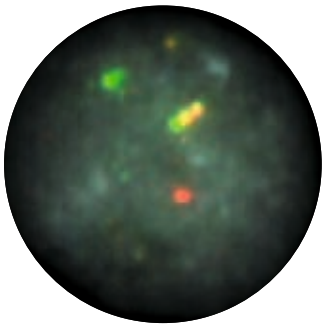
FGFR1 expression has been shown to play pivotal roles in mammary development and breast cancer tumorigenesis. It has been shown that FGFR1 amplification is found in up to 10% of breast cancers and is significantly more prevalent in patients older than 50 years of age and in tumors that lack HER2 expression.

Even though the prognostic impact of FGFR1 amplification in breast cancer still remains unclear, the functional data demonstrating that FGFR1 signaling is required for the survival of breast cancer cells harboring FGFR1 amplification and the relatively high prevalence of FGFR1 amplification in breast cancer support the idea that this gene may be a useful therapeutic target for a subgroup of breast cancer patients with FGFR1 gene amplification.

The FGFR1 (8p12) break-apart probe is optimized to detect translocations involving the FGFR1 gene region at 8p12 in a dual-color, split assay on metaphase/interphase spreads and paraffin embedded tissue sections.

Cat.# KBI-10737 FGFR1 (8p12) Break





FGFR1 (8p12) Break probe hybridized to patient material showing a break at 8p12 (1RG1R1G).

Literature:
Smedley et al, 1998, Hum Mol Genet. 7; 627-642.
Sohal et al, 2001, Genes Chrom. Cancer 32; 155-163.
Kwak et al, J Clin Oncol., 27(26):4247-53.

Ordering information	*Color*	*Tests*	*Cat#*
ON FGFR1 (8p12) Break	red/green	10	KBI-10737

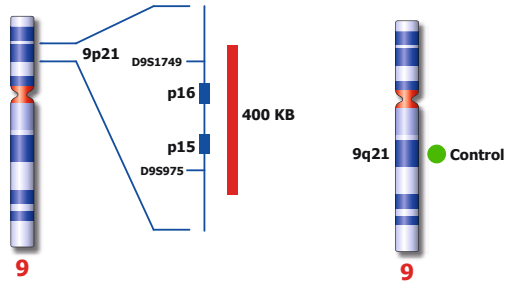
Bladder Cancer

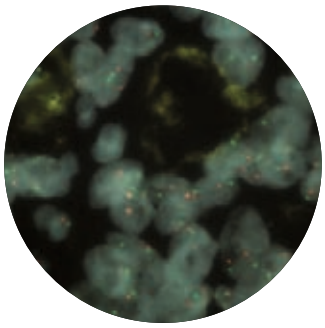
ON p16 (9p21) / 9q21 (tissue)

Homozygous and hemizygous deletions of 9p21 are the earliest and most common genetic alteration in bladder cancer. The p16 (INK4A) gene has been identified as tumor suppressor gene in this region which is commonly deleted in bladder cancer. The loss of DNA sequences on chromosomal bands 9p21-22 has been documented also in a variety of malignancies including leukemias, gliomas, lung cancers, and melanomas.

The p16 (9p21) specific DNA probe is optimized to detect copy numbers of the p16 gene region at region 9p21. The 9q21 region probe is included to facilitate chromosome identification.

Cat.# KBI-10710 p16 (9p21) / 9q21 (tissue)





p16 (9p21) / 9q21 (tissue) probe hybridized to tissue (2R2G).

Literature:

Stadler et al, 1994, Cancer Res, 54: 2060-2063.
Williamson et al, 1995, Hum Mol Genet, 4: 1569-1577.

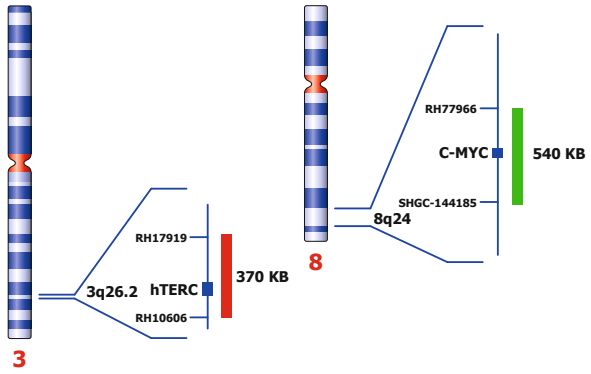
Ordering information	Color	Tests	Cat#
ON p16 (9p21) / 9q21 (tissue)	red/green	10	KBI-10710

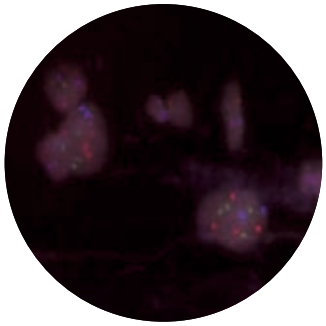
Cervical Cancer

ON CC hTERC (3q26) / C-MYC (8q24) / SE 7 TC

Cervical cancer, a potentially preventable disease, remains the second most common malignancy in women worldwide. The most consistent chromosomal gain in aneuploid tumors of cervical squamous cell carcinoma mapped to chromosome arm 3q, including the human telomerase gene locus (hTERC) at 3q26. High-level copy number increases were also mapped to chromosome 8. Integration of HPV (Human Papilloma Virus) DNA sequences into C-MYC chromosomal regions have been repeatedly observed in cases of invasive genital carcinomas and in cervical cancers. The hTERC (3q26) specific DNA Probe is optimized to detect copy numbers of the hTERC gene region at region 3q26. The C-MYC (8q24) specific DNA probe is optimized to detect copy numbers of the C-MYC gene region at 8q24. The chromosome 7 satellite enumeration probe (SE 7) at D7Z1 is included as ploidy control.

Cat.# KBI-10704 Cervical Cancer hTERC (3q26) / C-MYC (8q24) / SE 7 Triple-Color





CC hTERC (3q26) / C-MYC (8q24) / SE 7 TC probe hybridized to a PAP smear (destained) showing 3q26 and 8q24 amplification. The SE 7 control probe indicates a non-triploid karyotype (2B).
Image kindly provided by Dr. Weimer, Kiel.

Literature:

Xie et al, 2008, Geburtshilfe Frauenheilkunde, 68: 573.
Heselmeyer et al, 1996, PNAS, 93: 479-484.
Herrick et al, 2005, Cancer Res, 65: 1174-1179.

Ordering information	Color	Tests	Cat#
ON CC hTERC (3q26) / C-MYC (8q24) / SE 7 TC	red/green	10	KBI-10704

Lung Cancer

Lung cancer remains the leading cause of cancer death, annually resulting in more than one million cases worldwide. About 1.3 million new cases are diagnosed each year and prognoses are poor. Non-small cell lung cancer (NSCLC), the most common form (~80%) of lung cancer, has a 5-year survival rate of approximately 15%, mainly of late-stage detection[1].

A personalized medicine approach for treatment of NSCLC is emerging. Promising results have been obtained with specific anaplastic lymphoma kinase or ALK inhibitors like Crizotinib (Xalkori®)[2] in patients carrying the fusion gene ALK-EML4[3].

Literature:

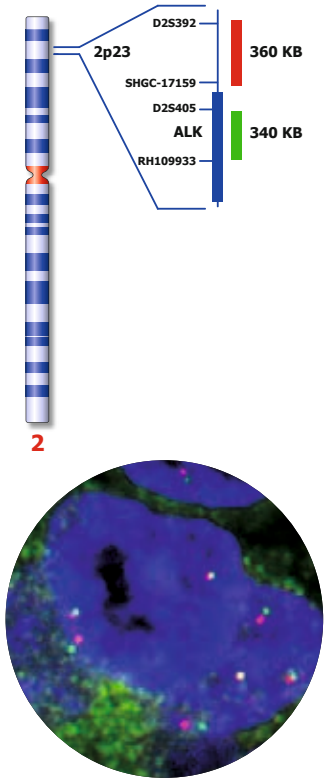
1. World Health Organization (Cancer Fact sheet N°297 2009: http://www.who.int/mediacentre/factsheets/fs297/en/
2. Kwak et al, J Clin Oncol., 27(26):4247-53
3. Koivunen et al, Clin Cancer Res, 2008, 14, 4275-4283

ON ALK (2p23) Break

Translocations of the ALK (anaplastic lymphoma kinase) gene at 2p23 have originally been associated with anaplastic lymphomas, B-cell lymphomas, neuroblastomas and myofibroblastic tumors. To date at least 21 translocation partners have been described, however 80% of the translocations involves the NPM1 gene (5q35). More recently ALK rearrangements have been described in non-small cell lung cancer (NSCLC) cases. Promising results have been obtained with specific anaplastic lymphoma kinase or ALK inhibitors like Crizotinib (Xalkori®) in patients carrying the fusion gene ALK-EML4.

The ALK (2p23) Break probe is optimized to detect translocations involving the ALK gene region at 2p23.

Cat# KBI-10747 ALK (2p23) Break



ALK (2p23) Break probe hybridized to lung adenocarcinoma tissue showing translocation involving the ALK region at 2p23 (1RG1R1G).
Image kindly provided by Prof. B. Terris, Dr. P.A. Just, Hôpital Cochin, Paris.

Literature:
Soda et al., Nature, 2007, 448, 561-566.
Kwak et al, J Clin Oncol., 27(26):4247-53.
Koivunen et al. Clin Cancer Res, 2008, 14, 4275-4283.

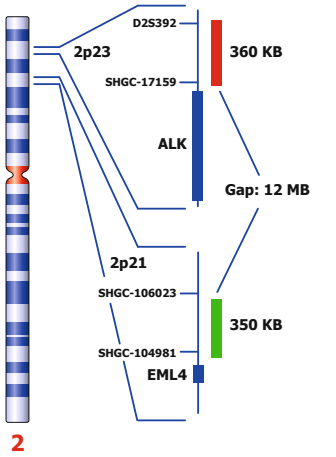
Ordering information	*Color*	*Tests*	*Cat#*
ON ALK (2p23) Break	red/green	10	KBI-10747

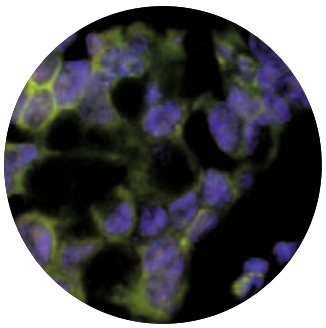
ON ALK/EML4 t(2;2); inv(2) Fusion

The inversion in 2p21 and 2p23 leading to a fusion of the kinase domain of ALK (anaplastic lymphoma kinase) and EML4 (echinoderm microtubule associated protein like 4) has been described in 5-7% of non-small cell lung cancer (NSCLC) cases. ALK and EML4 are ~12 MB apart in opposite directions; a simple inversion generates the fusion gene.
Promising results have been obtained with specific anaplastic lymphoma kinase or ALK inhibitors like Crizotinib (Xalkori®) in patients carrying the fusion gene ALK-EML4.

The ALK/EML4 t(2;2); inv(2) Fusion probe is designed as a dual-color assay to detect the fusion of the ALK gene with the EML4 gene by paracentric inversion with breakage and reunion occurring at bands 2p21 and 2p23.

Cat# KBI-10746 ALK/EML4 t(2;2); inv(2) Fusion





ALK/EML4 t(2;2); inv(2) Fusion probe hybridized to lung adenocarcinoma tissue showing ALK-EML4 fusion (2RG1R1G).
Image kindly provided by Prof. B. Terris, Dr. P.A. Just, Hôpital Cochin, Paris.

Literature:
Soda et al., Nature, 2007, 448, 561-566.
Koivunen et al. Clin Cancer Res, 2008, 14, 4275-4283.

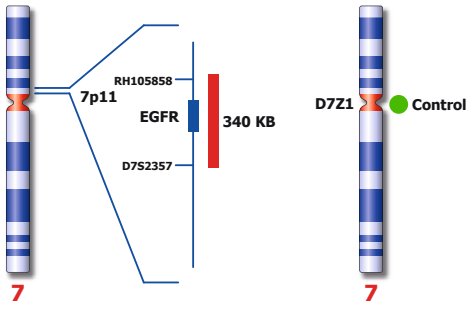
Ordering information	Color	Tests	Cat#
ON ALK/EML4 t(2;2); inv(2) Fusion	red/green	10	KBI-10746

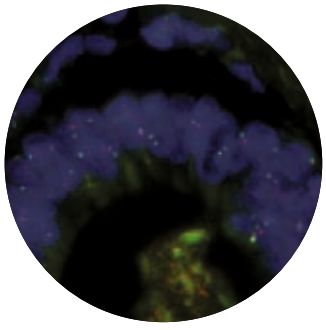
ON EGFR, Her-1 (7p11) / SE 7

Epidermal growth factor receptor (EGFR) is a cell membrane protein, providing signal transduction and cell growth. It is a member of the Her or Erb-B family of type I receptor tyrosine kinases and implicated in the development and progression of non-small cell lung carcinomas (NSCLC), breast, intestine, and other organs. EGFR has been found to act as a strong prognostic indicator in head and neck, ovarian, cervical, bladder and oesophageal cancers. In these cancers, increased EGFR expression was associated with reduced recurrence-free or overall survival.

The EGFR (7p11) specific DNA Probe is optimized to detect copy numbers of the EGFR (Her-1) gene region at region 7p11. The chromosome 7 satellite enumeration (SE) probe is included to facilitate chromosome identification.

Cat.# KBI-10702 EGFR, Her1 (7p11) / SE 7





EGFR, Her1 (7p11) / SE 7 hybridized to colon tissue (2R2G).

Literature:
Wang et al, 1993, Jpn J Hum Genet, 38: 399-406.
Nicholoson et al, 2001, Eur J Cancer, 37: 9-15.

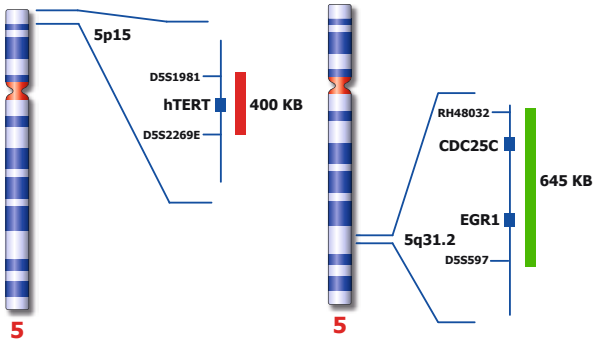
Ordering information	Color	Tests	Cat#
ON EGFR, Her-1 (7p11) / SE 7	red/green	10	KBI-10702

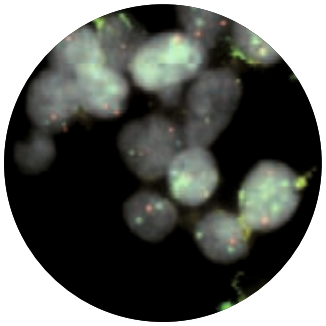
ON hTERT (5p15) / 5q31 (tissue)

Amplification of the hTERT gene at band 5p15 has been observed in a variety of cancer, particularly lung cancer, cervical tumors, and breast carcinomas. Several studies have revealed a high frequency of hTERT gene amplification in human tumors, which indicates that the hTERT gene may be a target for amplification during the transformation of human malignancies and that this genetic event probably contributes to a dysregulation of hTERT/ telomerase occurring in a subset of human tumors.

The hTERT (5p15) probe is designed as a dual-color assay to detect amplification at 5p15. The CDC25C/EGR1 (5q31) gene region probe is included as internal control.

Cat.# KBI-10709 hTERT (5p15) / 5q31 (tissue)





hTERT (5p15) / 5q31 (tissue) probe hybridized to paraffine embedded tissue (2R2G).

Literature:

Bryce et al, 2000, Neoplasia, 2; 197-201.
Zhang et al, 2000, Cancer Res, 60; 6230-6235.

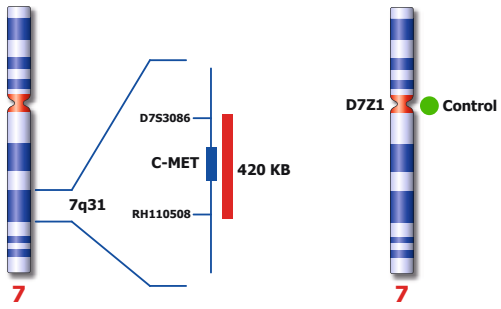
Ordering information	*Color*	*Tests*	*Cat#*
ON hTERT (5p15) / 5q31 (tissue)	red/green	10	KBI-10709

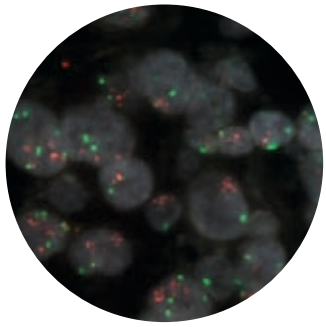
ON C-MET (7q31) / SE 7

The C-MET proto-oncogene is a receptor-like tyrosine kinase that drives a physiological cellular program important for development, cell movement, cell repair, cellular growth. Aberrant execution of this program has been associated to neoplastic transformation, invasion and metastasis. Activation of C-MET has been reported in a significant percentage of human cancers including non-small cell lung cancer (NSCLC). And is amplified during the transition between primary tumors and metastasis.

The C-MET (7q31) specific DNA probe is optimized to detect copy numbers of the C-MET gene region at region 7q31. The Chromosome 7 Satellite enumeration probe (SE 7) at D7Z1 is included to facilitate chromosome identification.

Cat.# KBI-10719 C-MET (7q31) / SE 7





Hybridization of MET Amplification Probe (KBI-10719) to a tissue section showing MET amplification.

Literature:

Go et al, 2010, J Thorac Oncol 5: 305-313.
Hara et al, 1998, Lab Invest 78; 1143-1153.
Tsugawa et al., 1998, Oncology 55; 475-481.

Ordering information	*Color*	*Tests*	*Cat#*
ON C-MET (7q31) / SE 7	red/green	10	KBI-10719

Prostate Cancer

Prostate cancer is the most commonly diagnosed, nondermatological malignancy in men; causing death in about 1 out of 35 Western men. Prostate cancer is the second leading cause of cancer death behind lung cancer.[1]

Lately, great advances have been made using genomic technologies to develop predictive models that anticipate the risk of developing prostate cancer, prostate cancer progression, and the response of prostate cancer to therapy.[2]

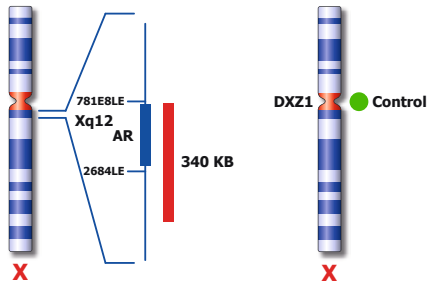
Literature:
1. American Cancer Society: http://www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-key-statistics, revision of 11/22/2010, accessed on Dec 13, 2010.
2. Febbo, P.G., 2009, Cancer, 115: 3046-3057.

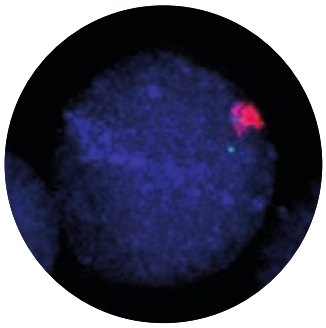
ON AR (Xq12) / SE X

The androgen receptor (AR) gene has been identified as a target gene for the Xq12 amplification found in one-third of hormone-refractory prostate cancers. The findings suggest that the AR gene amplification and overexpression is involved in the emergence of prostate cancer.

The AR (Xq12) specific DNA Probe is optimized to detect copy numbers of the AR gene region at region Xq12. The chromosome X satellite enumeration probe (SE X) at DXZ1 is included to facilitate chromosome identification.

Cat# KBI-10720 AR (Xq12) / SE X





AR (Xq12) / SE X probe hybridized to VCaP prostate cancer cell showing highlevel AR gene amplification.
Image kindly provided by Prof. Trapman, Erasmus Medical Centre, Rotterdam.

Literature:
Visakorpi T et al, 1995, Nat. Genet. 9; 401-406.
Koivisto P et al, 1997, Cancer Res. 57 ; 314-319.

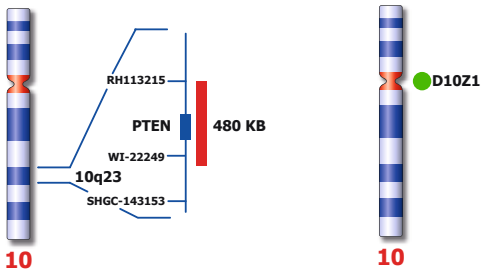
Ordering information	*Color*	*Tests*	*Cat#*
ON AR (Xq12) / SE X	red/green	10	KBI-10720

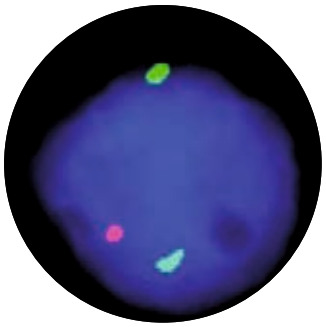
ON PTEN (10q23) / SE 10

The gene 'phosphatase and tensin homolog deleted on chromosome 10' (PTEN), is a tumor suppressor located at chromosome 10q23, that plays an essential role in the maintenance of chromosomal stability, cell survival and proliferation. Loss of PTEN has been found in a wide number of tumors, and his important role is demonstrated by the fact that it is the second most frequently mutated gene after p53. Loss of PTEN significantly correlates with the advanced forms of gliomas, but also of prostate cancer and breast tumors.

The PTEN (10q23) specific DNA probe is optimized to detect copy numbers of the PTEN gene region at region 10q23. The Chromosome 10 Satellite enumeration probe (SE 10) at D10Z1 is included to facilitate chromosome identification.

Cat.# KBI-10718 PTEN (10q23) / SE 10





PTEN (10q23) / SE 10 probe hybridized to prostate cancer material showing deletion of PTEN gene region at 10q23 (1R2G).
Image kindly provided by Portuguese Cancer Inst., Porto.

Literature:

Cairns et al, 1997, Cancer Res, 57 ; 4997-5000.
Hermans et al, 2004, Genes Chrom Cancer, 39; 171-184.

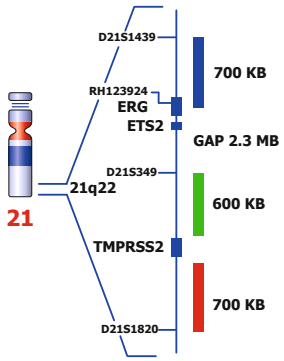
Ordering information	*Color*	*Tests*	*Cat#*
ON PTEN (10q23) / SE 10	red/green	10	KBI-10718

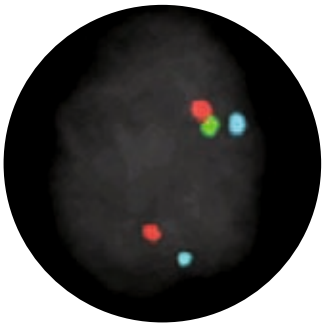
ON TMPRSS2-ERG (21q22) Del, Break, TC

The transmembrane protease serine 2 gene (TMPRSS2) is involved in gene fusions with ERG, ETV1 or ETV4 in prostate cancer. In recent studies it has been reported that the expression of the TMPRSS2-ERG fusion gene is a strong prognostic factor for the risk of prostate cancer recurrence in prostate cancer patients treated by surgery.

The TMPRSS2-ERG rearrangement probe is optimized to detect the deletion between TMPRSS2 and ERG at 21q22 associated with the TMPRSS2-ERG fusion in a triple-color deletion assay. It also detects translocations involving the TMPRSS2 region such as ETV1 t(7;21), or ETV4 t(17;21).

Cat.# KBI-10726 TMPRSS2-ERG (21q22) Del, Break, TC





TMPRSS2-ERG (21q22) rearrangement probe hybridized to prostate carcinoma tissue showing a deletion of the TMPRSS2 (21q22) gene region associated with TMPRSS2-ERG fusion (1RGB 1RB).
Image kindly provided by Dr. Teixeira, Porto.

Literature:

Perner et al, 2006 Cancer Res 66; 8337-8341.
Hermans et al, 2006, Cancer Res 66; 10658-10663.
Attard et al, 2008, Oncogene 27; 253-263.

Ordering information	*Color*	*Tests*	*Cat#*
TMPRSS2-ERG (21q22) Del, Break, TC	red/green	10	KBI-10726

Thyroid Carcinoma

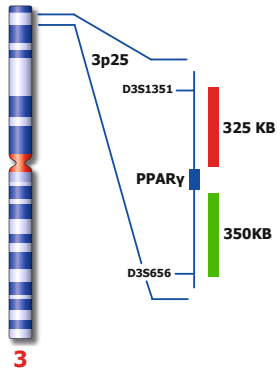
Papillary thyroid carcinoma (PTC) is the most frequent primary carcinoma of the thyroid gland. PTC, conversely, is multifocal and are associated with prior radiation and high iodine intake. The follicular carcinomas is associated with endemic goiter and a diet with low iodine intake.

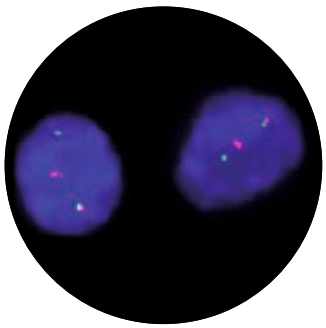
ON PPARγ (3p25), Break

Follicular thyroid carcinoma is associated with the chromosomal translocation t(2;3)(q13;p25), fusing PAX8 (2q13) with the nuclear receptor, peroxisome proliferator-activated receptor γ (PPARγ). PPAR is located in a breakpoint hot spot region, leading to recurrent alterations of this gene in thyroid tumors of follicular origin including carcinomas as well as adenomas with or without involvement of PAX8.

A break or split probe for PPARγ is best used to analyze translocation of the PPARγ (3p25) gene on formalin fixed paraffin embedded tissue for routine clinical diagnosis.

Cat.# KBI-10707 PPARγ (3p25) Break





PPARγ (3p25) Break probe hybridized to patient material showing a translocation at 3p25 (1RG1R1G).
Image kindly provided by Dr. Valent, Paris.

Literature:

French et al, 2003, Am J Pathol, 162; 1053-1060.
Drieschner et l, 2006, Thyroid, 16; 1091-1096.

Ordering information	Color	Tests	Cat#
ON PPARγ (3p25), Break	red/green	10	KBI-10707

Neuroblastoma

According to the International Neuroblastoma Risk Grouping (INRG) Biology Committee MYCN remains the only genomic factor to be used currently for treatment stratification. Common data elements to be obtained by all groups include tumor cell ploidy and copy number/ LOH status at chromosome bands 1p36, 11q23, and 17q23-25.

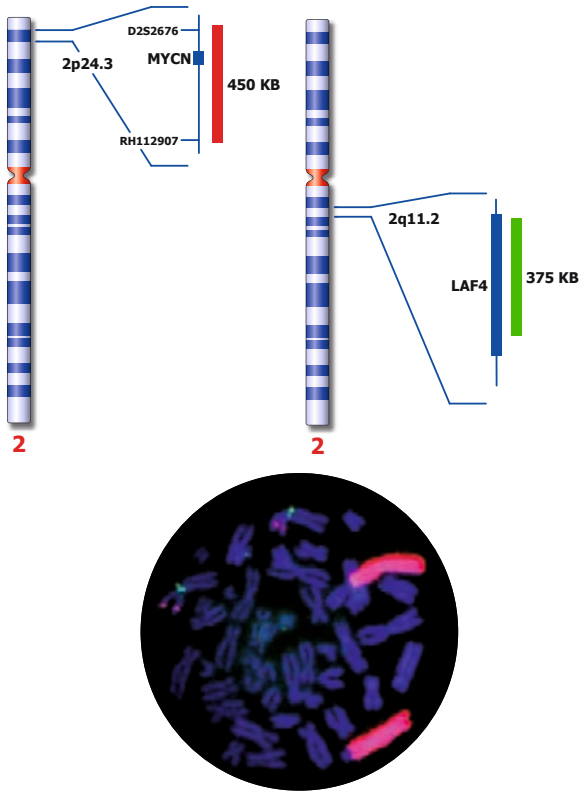
Literature:
Ambros et al, 2006, Advances in Neuroblastoma Research.

ON MYCN (2p24) / LAF (2q11)

Amplification of the human N-myc protooncogene, MYCN, is frequently seen either in extrachromosomal double minutes or in homogeneously staining regions of aggressively growing neuroblastomas. MYCN amplification has been defined by the INRG as > 4-fold MYCN signals compared to 2q reference probe signals.

The MYCN (2p24) specific DNA probe is optimized to detect copy numbers of the MYCN gene region at 2p24. The LAF gene region probe at 2q11 is included to facilitate chromosome identification.

Cat.# KBI-10706 MYCN (2p24) / LAF (2q11)



MYCN (2p24) / LAF (2q11) hybridized to a cell line showing amplification of MYCN on chromosome 13 and 15.
Image kindly provided by Pasteur Workshop 2008, Paris.

Literature:
Shapiro et al, 1993, Am J Pathol, 142: 1339-1346.
Corvi et al, 1994, PNAS, 91: 5523-5527.

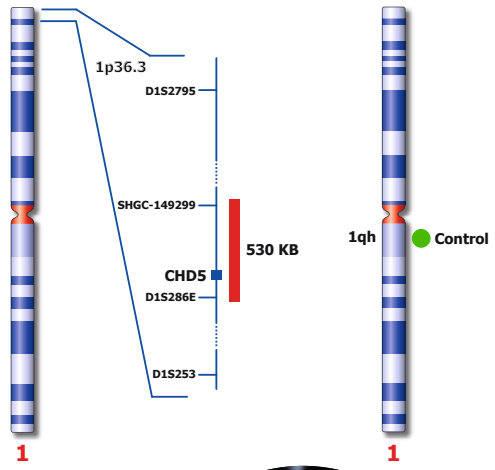
Ordering information	*Color*	*Tests*	*Cat#*
ON MYCN (2p24) / LAF (2q11)	red/green	10	KBI-10706

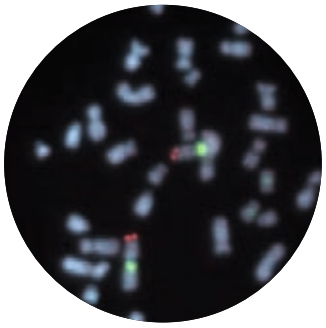
ON SRD 1p36 / SE 1(1qh)

Neuroblastomas frequently have deletions of chromosome 1p and amplification of the N-myc oncogene. These deletions tend to be large and extend to the telomere, but a common region within sub-band 1p36.3 is consistently lost in these deletions. Inactivation of a tumor suppressor gene within 1p36.3 is believed to be associated with an increased risk for disease relapse. The 1p36 specific DNA probe has recently been changed to cover the recently described smallest region of consistent deletion **(SRD)** between D1S2795 and D1S253.

The SRD (1p36) specific DNA probe is optimized to detect copy numbers of the 1p36 region on chromosome 1. The chromosome 1 satellite enumeration probe (SE 1) at 1qh is included to facilitate chromosome identification.

Cat.# KBI-10712 SRD (1p36) / SE 1(1qh)





SRD (1p36) / SE 1 probe hybridized to a normal metaphase (2R2G).

Literature:
Caron et al, 1993, Nat Genet, 4: 187-190.
Cheng et al, 1995, Oncogene, 10: 291-297.
White et al, 2005, Oncogene, 24: 2684-2694.

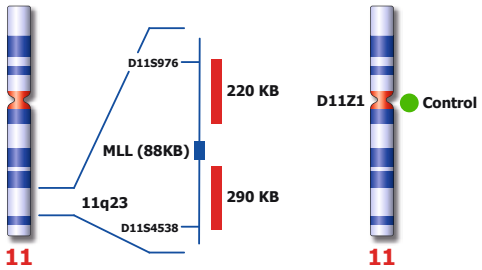
Ordering information	Color	Tests	Cat#
ON SRD (1p36) / SE1(1qh)	red/green	10	KBI-10712

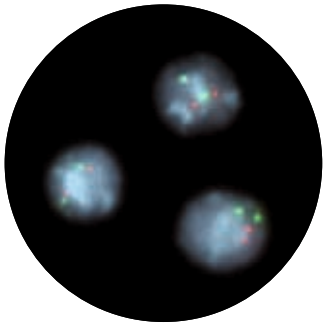
ON MLL (11q23) / SE 11

Deletions of the long arm of chromosome 11 (11q) have been noted in primary neuroblastomas. It is assumed that a tumor suppressor gene mapping within 11q23.3 is commonly inactivated during the malignant evolution of a large subset of neuroblastomas, especially those with unamplified MYCN.

The MLL (11q23) specific DNA probe is optimized to detect amplification or deletion involving the MLL gene region at 11q23 in a dual-color assay on metaphase/interphase spreads, blood smears and bone marrow cells. The Chromosome 11 Satellite Enumeration probe (SE 11) at D11Z1 is included to facilitate chromosome identification.

Cat.# KBI-10711 MLL (11q23) / SE 11





MLL (11q23) / SE 11 hybridized to normal interphases (2R2G).

Literature:
Guo et al, 1999, Oncogene, 18: 4948-4957.
Maris et al, 2001, Med Pediatr Oncol, 36: 24-27.

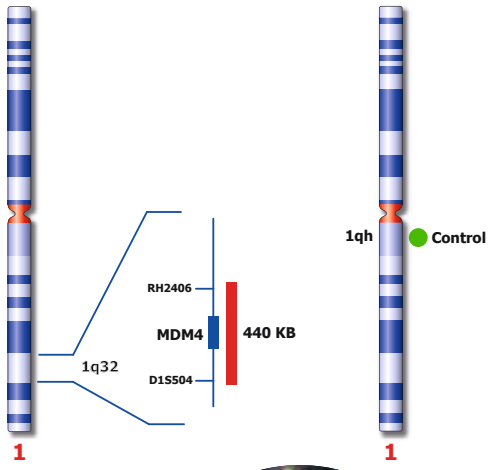
Ordering information	Color	Tests	Cat#
ON MLL (11q23) / SE11	red/green	10	KBI-10711

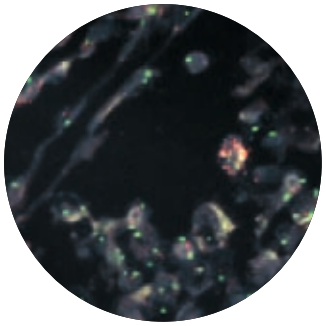
ON MDM4 (1q32) / SE1

MDM4 (also known as MDMX, murine double minute gene) is a relative of MDM2 that was identified on the basis of its ability to physically interact with p53. MDM4, like MDM2, acts as a key negative supressor of p53 by interfering with its transcriptional activity. MDM4 amplification and/or overexpression occurs in several diverse tumors. Studies showed an increased MDM4 copy number in 65% of human retinoblastomas compared to other tumors, qualifying MDM4 as a specific chemotherapeutic target for treatment of this tumor.

The MDM4 (1q32) specific DNA probe is designed as a dual-color assay to detect amplification at 1q32. The chromosome 1 Satellite Enumeration (SE 1) probe at 1qh is included to facilitate chromosome identification.

Cat.# KBI-10736 MDM4 (1q32) / SE 1





MDM4 (1q32) / SE 1 probe hybridized to paraffin embedded tissue (2R2G).

Literature:

Riemenschneider et al, 1999, Cancer Res. 59 ; 6091-6096.
Danovi et al, 2004, Mol.Cell.Bio. 24; 5835-5843.

Ordering information	*Color*	*Tests*	*Cat#*
ON MDM4 (1q32) / SE 1	red/green	10	KBI-10736

Sarcoma

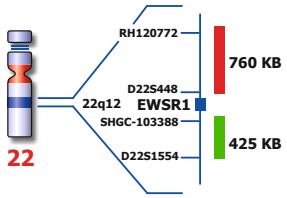
Sarcoma is a general class of less common cancers in which the cancer cells arise from or resemble normal cells in the body known as "connective tissues" (fat, muscle, blood vessels, deep skin tissues, nerves, bones, and cartilage). The benign and malignant forms have related karyotypic changes which provide an important resource for identifying the additional genetic changes that occur in the malignant compared with the benign form. In fact, the molecular biology of soft-tissue sarcomas has provided the perfect example of how cytogenetic and molecular approaches can contribute toward a clearer understanding of the development of soft-tissue sarcomas.

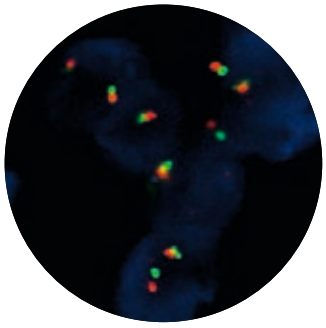
ON EWSR1 (22q12) Break

Ewing's sarcoma is the second most frequent primary bone cancer. In most cases a translocation involving the EWSR1 gene at 22q12 and the FLI1 gene at 11q24 are observed, but several other translocation partners (ERG, ETV1, FEV, and E1A3) can also be involved.

The EWSR1 (22q12) Break Probe is optimized to detect translocations involving the EWSR1 gene region at 22q12 in a dual-color, split assay on metaphase/interphase spreads and paraffin embedded tissue sections.

Cat.# KBI-10750 EWSR1 (22q12) Break





Interphase FISH result of the EWSR1 split probe. Co-localisation indicates intact EWSR1 locus, separation of the green and red signal indicates the presence of a translocation breakpoint.

Literature:

Zucman-Rossi, et al, 1998, PNAS, 95; 11786-11791.
Bernstein et al, 2006, Oncologist, 11; 503-519.

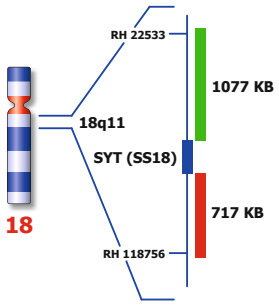
Ordering information	*Color*	*Tests*	*Cat#*
ON EWSR1 (22q12) Break	red/green	10	KBI-10750

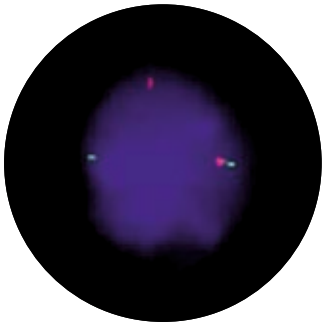
ON SYT (18q11) Break

The characteristic chromosomal abnormality in synovial sarcoma is t(X;18)(p11.2;q11.2) present in 90% of patients. This translocation results in the fusion of the chromosome 18 SYT gene to either of two distinct genes, SSX1 or SSX2, located on the X chromosome.

A break or split probe for SYT is best used to analyze translocation of the SYT (SS18) gene on formalin fixed paraffin embedded tissue for routine clinical diagnosis.

Cat.# KBI-10713 SYT (18q11) Break





SYT (18q11) Break probe hybridized to patient material showing translocation of the SYT (SS18) gene region at 18q11 (1RG1R1G).

Literature:
Kawai et al, 1998, NEJM, 338; 153-160.
Surace et al, 2004, LabInvest., 84; 1185-1192.

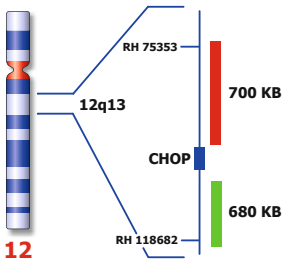
Ordering information	*Color*	*Tests*	*Cat#*
ON SYT (18q11) Break	red/green	10	KBI-10713

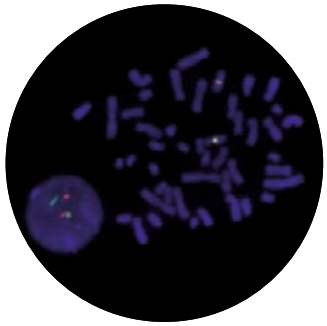
ON CHOP (12q13) Break

Liposarcoma is one of the most frequent sarcomas in adults, representing 10 to 16 percent of soft tissue sarcomas. Most patients with round cell/myxoid liposarcoma have an acquired t(12;16)(CHOP-FUS) or t(12;22)(CHOP-EWS) translocation, both of which involve the CHOP gene at 12q13. A break or split probe for CHOP is best used to analyze translocation of the CHOP (12q13) gene on formalin fixed paraffin embedded tissue for routine clinical diagnosis.

The CHOP (12q13) Break probe is optimized to detect translocations involving the CHOP gene region at 12q13 in a dual-color, split assay.

Cat.# KBI-10714 CHOP (12q13) Break





CHOP (12q13) Break probe hybridized to a normal metaphase (2RG).

Literature:
Panagopoulos et a, 1994, Cancer Res, 54; 6500-6503.
Schoenmakers et al, 1994, Genomics, 20; 210-222.

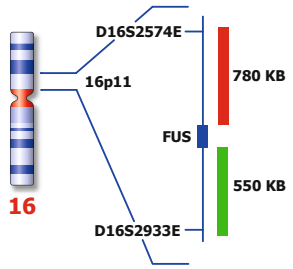
Ordering information	*Color*	*Tests*	*Cat#*
ON CHOP (12q13) Break	red/green	10	KBI-10714

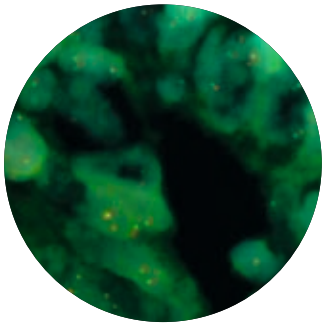
ON FUS (16p11) Break

The FUS gene was originally shown to be rearranged in myxoid liposarcomas harboring a t(12;16)(q13;p11) translocation.
FUS has also been shown to be involved in other recombinations: with ERG in acute myeloid leukemia carrying a t(16;21), with ATF1 in band 12q13 in angiomatoid fibrous histiocytoma, and with CREB3L2 in fibromyxoid sarcoma.

A break or split probe for FUS is best used to analyze translocation of the FUS (16p11) gene on formalin fixed paraffin embedded tissue for routine clinical diagnosis.

Cat.# KBI-10715 FUS (16p11)





FUS (16p11) Break probe hybridized to liposarcoma material.

Literature:
Shing et al, 2003, Cancer Res, 63: 4568-4576.
Storlazzi et al, 2003, Hum. Mol. Genet., 12: 2349-2358.

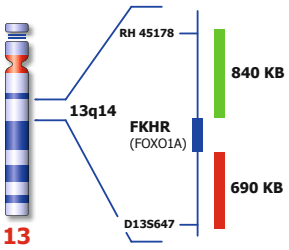
Ordering information	Color	Tests	Cat#
ON FUS (16p11), Break	red/green	10	KBI-10715

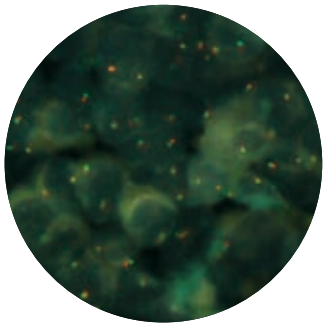
ON FKHR (13q14) Break

The t(2;13) is associated with alveolar rhabdomyosarcomas. This translocation results in the formation of a chimeric transcript consisting of the 5' portion of PAX3, including an intact DNA-binding domain fused to the FKHR gene on chromosome 13. The t(1;13)(p36;q14) also seen in alveolar rhabdomyosarcomas results in the fusion of another member of the PAX family, PAX7 to the FKHR gene on chromosome 13.

A break or split probe for FKHR is best used to analyze translocation of the FKHR (13q14) gene on formalin fixed paraffin embedded tissue for routine clinical diagnosis.

Cat.# KBI-10716 FKHR (13q14) Break





FKHR (13q14) Break probe hybridized to patient material.

Literature:
Barr et al, 1996, Hum. Mol. Genet., 5; 15-21.
Coignet et al, 1999, Genes Chrom. Cancer, 25; 222-229.

Ordering information	Color	Tests	Cat#
ON FKHR (13q14) Break	red/green	10	KBI-10716

ON MDM2 (12q15) / SE 12

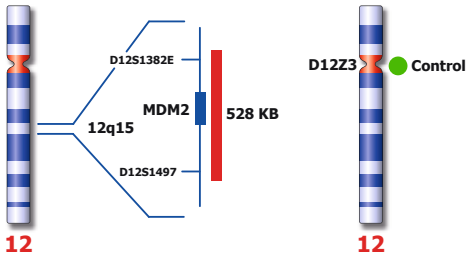
Well-differentiated liposarcoma/atypical lipomatous tumor and dedifferentiated liposarcoma are among the most common malignant soft tissue tumors presented in older adults. These tumors can be difficult to distinguish from benign lipomatous neoplasms and other high-grade sarcomas.

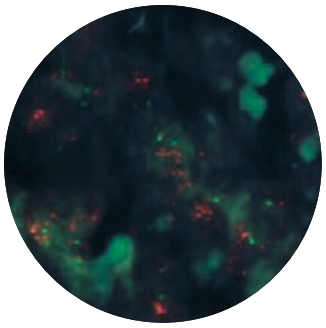
Amplification of the MDM2 gene has been identified in lipomatous neoplasms. The use of fluorescence in situ hybridization in identifying MDM2 amplification has made the MDM2 amplification probe a valuable diagnostic tool in well-differentiated liposarcomas/atypical lipomatous tumors.

Fibrosarcoma is a rare soft-tissue tumor composed of fascicles of spindled fibroblast-like cells. Gains and high-level amplifications of 12q14–22 were the most common genomic imbalances, and reflected MDM2 amplification, thereby indicating the importance of this gene in the evolution of fibrosarcomas.

The MDM2 (12q15) specific DNA probe is optimized to detect copy numbers of the MDM2 gene region at region 12q15. The Chromosome 12 Satellite Enumeration probe (SE 12) at D12Z3 is included to facilitate chromosome identification.

Cat.# KBI-10717 MDM2 (12q15) / SE 12





MDM2 (12q15) / SE 12 Amplification probe hybridized to patient material showing amplification of the MDM2 gene region at 12q15.

Literature:
Uchida et al., 2010, Cancer Genet Cytogenet 203; 324-327.
Lucas et al, 2010, Am J Surg Pathol 34: 844-851.
Weaver et al, 2008, Mod Pathol 21: 943-949.
Mitchell et al, 1995, Chrom. Res., 3; 261-262.
Reifenberger et al, 1996, Cancer Res., 15; 5141-5145.

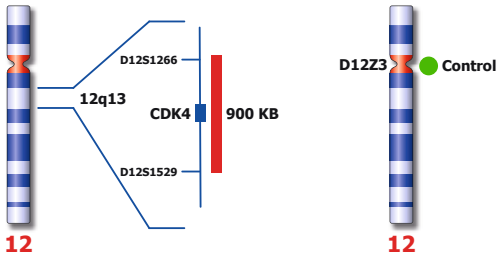
Ordering information	*Color*	*Tests*	*Cat#*
ON MDM2 (12q15) / SE12	red/green	10	KBI-10717

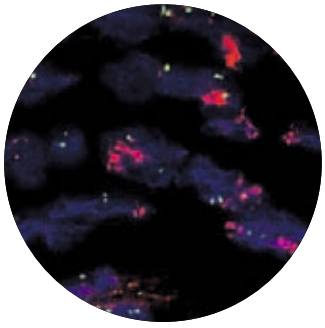
ON CDK4 (12q13) / SE 12

Amplification of the CDK4 gene region at 12q13-q15 has been observed in several types of cancer, especially in gliomas and sarcomas. CDK4 codes for a cyclin dependent kinase which is involved in controlling progression through the G1 phase of the cell cycle. The oncogenic potential of CDK4 activation has been related to the deregulation of the G1 phase by increasing the hyperphosphorylation of retinoblastoma tumor suppressor protein helping to cancel its growth-inhibitory effects.

The CDK4 (12q13) specific DNA probe is optimized to detect copy numbers of the CDK4 gene region at 12q13. The chromosome 12 satellite enumeration probe (SE 12) at D12Z3 is included to facilitate chromosome identification.

Cat.# KBI-10725 CDK4 (12q13) / SE 12





CDK4 (12q13) / SE 12 probe hybridized to liposarcoma tissue showing multiple amplification involving the CDK4 gene region at 12q13 (3+R2G). Image kindly provided by Dr. Sapi, Hungary.

Literature:
Kuhnen et al, 2002, Virchows Arch 441 ; 299-302.
Shimada et al, 2006, Hum Path 37(9) ; 1123-1129.

Ordering information	Color	Tests	Cat#
ON CDK4 (12q13) / SE 12	red/green	10	KBI-10725

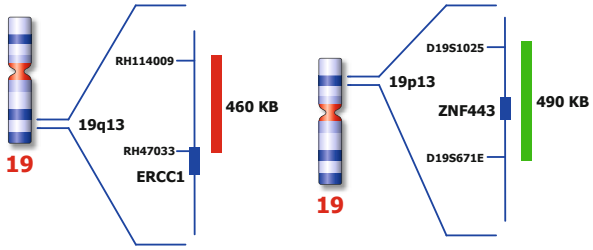
Different Cancer types

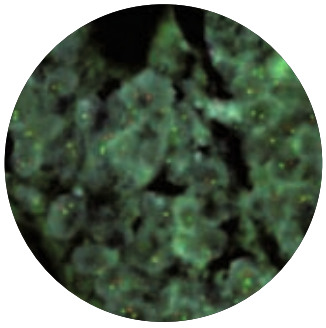
ON ERCC1 (19q13) & ZNF443 (19p13)

Nucleotide excision repair (NER) is the primary DNA repair mechanism that removes platinum-DNA adducts from genomic DNA. Excision repair cross-complementing rodent repair deficiency, complementation group 1 (ERCC1) is a critical gene in the NER pathway. A growing list of reports links cisplatin, carboplatin, and oxaliplatin based chemotherapy resistance to ERCC1 expression levels in several tumors. This relationship has been suggested for patients with gastric, bladder, ovarian, colorectal and non–small-cell lung cancers (NSCLC). ERCC1 has been shown to be an important marker to predict responsiveness to cisplatin-based chemotherapy. Low ERCC1 gene expression correlates with prolonged survival after cisplatin-based chemotherapy.

The ERCC1 (19q13) specific DNA Probe has been optimized to detect copy numbers of the ERCC1 gene region at 19q13. The ZNF443 (19p13) probe is included to facilitate chromosome identification.

Cat.# KBI-10739 ERCC1 (19q13) & ZNF443 (19p13)





ERCC1 (19q13) & ZNF443 (19p13) probe hybridized to paraffin embedded tissue (2R2G).

Literature:
Olaussen et al, 2006, N. Engl. J. Med. 335; 983-991.
Ceppi et al, 2006, Ann. Oncol. 17; 1818-1825.

Ordering information	Color	Tests	Cat#
ON ERCC1 (19q13) / ZNF443 (19p13)	red/green	10	KBI-10739

ON AURKA (20q13) / 20q11

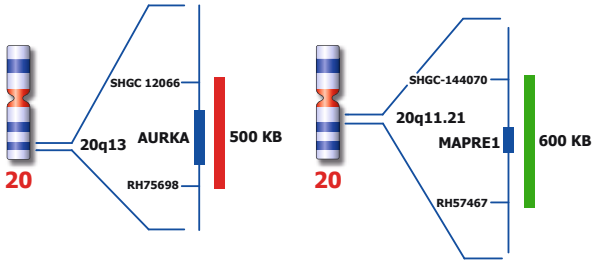
Aurora kinase A (AURKA) has the fundamental role of regulating proper centrosome function, important to maintain genomic stability during cell division and to ensure equal segregation of replicated chromosomes to daughter cells.

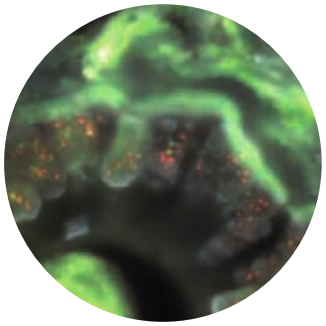
Deregulated duplication and distribution of centrosomes has been implicated in mechanisms leading to mitotic spindle aberrations, aneuploidy, and genomic instability that are seen in many different tumor types. Consistent with this, AURKA amplification has been detected in approximately 12% of primary breast tumors, as well as in breast, bladder, ovarian, colon, prostate, neuroblastoma and cervical cancer cell lines.

Recent investigations on new drugs developments have focused on the importance of aurora kinases for tumor suppression.

The AURKA (20q13) specific DNA probe is optimized to detect copy numbers of the AURKA gene region at region 20q13. The 20q11 specific DNA probe is included to facilitate chromosome identification.

Cat.# KBI-10721 AURKA (20q13) / 20q11





AURKA (20q13) / 20q11 probe hybridized to colorectal carcinoma material showing amplification of AURKA, gene region at 20q13.
Material kindly provided by Dr. Carvalho, Amsterdam.

Literature:

Uchida et al., 2010, Cancer Genet Cytogenet 203; 324-327.
Sen et al, 2002, J of Nat Canc Inst 94; 1320-1329.
Lassmann et al, 2007, Clin Cancer Res 13; 4083-4091.

Ordering information	*Color*	*Tests*	*Cat#*
ON AURKA (20q13) / 20q11	red/green	10	KBI-10721

ON AURKB (17p13) / SE 17

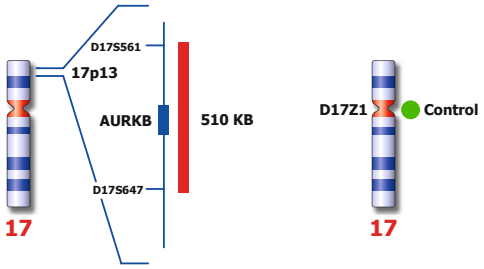
Aurora kinase B (AURKB) localizes to microtubules, and is a key regulator of the mitotic cell division and chromosome segregation processes. Gain of function of AURKB correlates with cell proliferation, induction of multinuclear cells, and chromosomal instability.

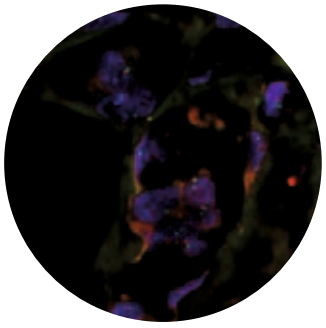
The significant interest of the gene in cancer diagnostics is related to the driving function of AURKB in tumor progression, histological differentiation, and metastasis. AURKB is predictive for the aggressive recurrence of many different types of tumors, including hepatocellular carcinoma and oral squamous cell carcinoma.

Recently new drugs have been under investigation for their capacity of interfering with the aurora kinases activity related to tumor-suppressor effects.

The AURKB (17p13) specific DNA probe is optimized to detect copy numbers of the AURKB gene region at region 17p13. The Chromosome 17 Satellite Enumeration (SE 17) probe at D17Z1 is included to facilitate chromosome identification.

Cat.# KBI-10722 AURKB (17p13) / SE 17





AURKB (17p13) / SE 17 probe hybridized to tumor tissue (2R2G).

Literature:

Smith et al, 2005, Br J Cancer, 93; 719-729.

Ordering information	*Color*	*Tests*	*Cat#*
ON AURKB (17p13) / SE 17	red/green	10	KBI-10722

ON CCND1 (11q13) / SE 11

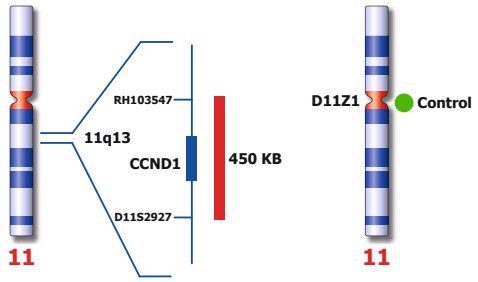
CCND1 (also named Cyclin D1 or BCL1) is a key cell cycle regulator of the G1 to S phase progression. The binding of cyclin D1 to cyclin-dependent kinase (CDKs) leads to the phosphorylation of retinoblastoma protein (pRb), subsequently triggering the release of E2F transcription factors to allow G1 to S phase progression of the cell cycle.

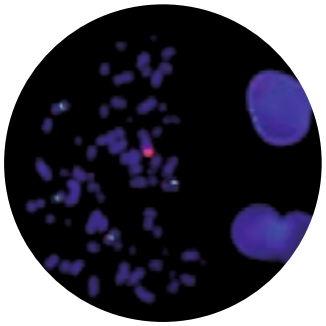
Consistent with this function, overexpression of cyclin D1 results in a more rapid progression from the G1 to S phase transition and in a reduced serum dependency in fibroblast cells, characteristics typically seen in cancer cells.

Amplification of cyclin D1 plays pivotal roles in the development of a subset of human cancers including parathyroid adenoma, breast cancer, colon cancer, lymphoma, melanoma, and prostate cancer.

The CCND1 (11q13) specific DNA Probe is optimized to detect copy numbers of the CCND1 gene region at region 11q13. The Chromosome 11 Satellite Enumeration (SE 11) probe at D11Z1 is included to facilitate chromosome identification.

Cat.# KBI-10734 CCND1 (11q13) / SE 11





CCDN1 (11q13) / SE 11 probe hybridized to patient interphases/ metaphase showing CCDN1 (11q13) amplification with polyploidy for chromosome 11.

Literature:

Okami et al, 1999, Oncogene 18; 3541-3545.
Freier et al, 2003, Cancer Res; 1179-1182.

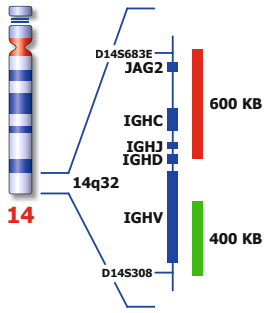
Ordering information	*Color*	*Tests*	*Cat#*
ON CCND1 (11q13) / SE 11	red/green	10	KBI-10734

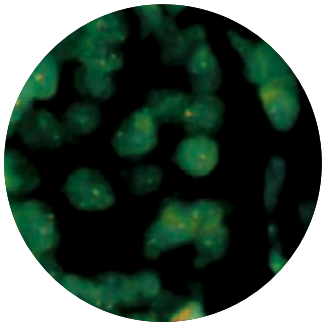
ON IGH (14q32) Break (tissue)

Chromosomal rearrangements involving the immunoglobulin heavy chain gene (IGH) at 14q32 are observed in 50% of patients with B-cell non-Hodgkin's lymphoma (NHL) and many other types of Lymphomas. More than 50 translocation partners with IGH have been described. In particular t(8;14), is associated with Burkitt's lymphoma, t(11;14) is associated with Mantle cell lymphoma, t(14;18) is observed in a high proportion of follicular lymphomas and t(3;14) is associated with Diffuse Large B-Cell Lymphoma.

The IGH (14q32) break probe is optimized to detect translocations involving the IGH gene region at 14q32 in a dual-color, split assay. Kreatech has developed this probe for the specific use on cell material (KBI-10601), or for the use on tissue (KBI-10729).

Cat.# KBI-10729 IGH (14q32) Break (tissue)





IGH (14q32) Break probe hybridized to patient material showing a partial deletion of 14q32 (1RG1R).

Literature:

Taniwaki et al, 1994, Blood, 83: 2962-1969.
Gozetti et al, 2002, Cancer Research, 62: 5523-5527.

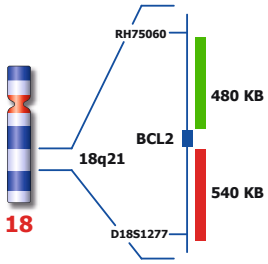
Ordering information	Color	Tests	Cat#
ON IGH (14q32) Break (tissue)	red/green	10	KBI-10729

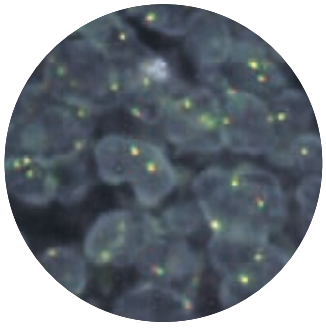
ON BCL2 (18q21) Break (tissue)

Follicular lymphoma is a mature B-cell lymphoma characterized by the presence of the t(14;18) translocation that juxtaposes the BCL2 locus on chromosome 18q21 to the immunoglobulin H (IGH) locus on chromosome 14q32, resulting in the overexpression of the anti-apoptotic protein BCL2. Next to IGH, additional translocation partners to BCL2 have been identified (e.g. IGK at 2p11.2 and IGL at 22q11). A break or split assay is therefore best suited to detect rearrangements of the BCL2 gene region at 18q21.

The BCL2 (18q21) Break probe is optimized to detect translocations involving the BCL2 gene region at 18q21 in a dual-color, split assay on paraffin embedded tissue sections. Kreatech has developed this probe for the specific use on cell material (KBI-10612), or for the use on tissue (KBI-10745).

Cat# KBI-10745 BCL2 (18q21) Break (tissue)





ON BCL2 (18q21) Break hybridized to paraffin embedded tissue (2RG).

Literature:

Taniwaki M et al, 1995, Blood, 86; 1481-1486.
Poetsch M et al, 1996, J Clin Oncol, 14; 963- 969.
Einerson R et al, 2005, Am J Clin Pathol, 124; 421-429.

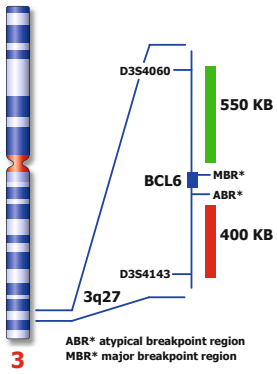
Ordering information	Color	Tests	Cat#
ON BCL2 (18q21) Break (tissue)	red/green	10	KBI-10745

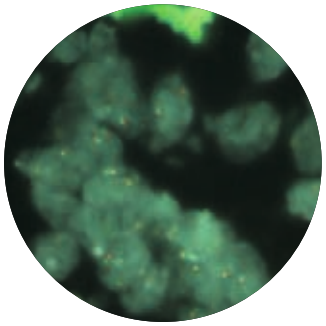
ON BCL6 (3q27) Break (tissue)

Chromosomal translocations involving band 3q27 with various different partner chromosomes represent a recurrent cytogenetic abnormality in B-cell non-Hodgkin's lymphoma. A FISH strategy using two differently labeled flanking BCL6 probes provides a robust, sensitive, and reproducible method for the detection of common and uncommon abnormalities of BCL6 gene in interphase nuclei. Kreatech has developed this probe for the specific use on cell material (KBI-10607), or for the use on tissue (KBI-10730).

Two different breakpoint regions have been identified; the major breakpoint region **(MBR)** is located within the 5' noncoding region of the BCL6 proto-oncogene, while the atypical breakpoint region **(ABR)** is located approximately 200 kb distal to the BCL6 gene. The BCL6 (3q27) Break probe is designed to flank both possible breakpoints, thereby providing clear split signals in either case.

Cat.# KBI-10730 BCL6 (3q27) Break (tissue)





BCL6 (3q27) Break probe hybridized to patient material showing both normal (2RG) and aberrant signals (1RG1R1G).
Image kindly provided by Prof Siebert, Kiel.

Literature:

Butler et al, 2002, Cancer Res, 62; 4089-4094.
Sanchez-Izquierdo, 2001, Leukemia, 15; 1475-1484.

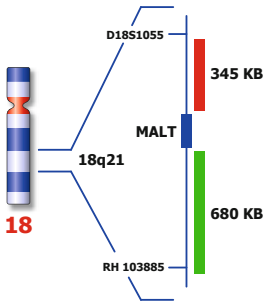
Ordering information	*Color*	*Tests*	*Cat#*
ON BCL6 (3q27) Break (tissue)	red/green	10	KBI-10730

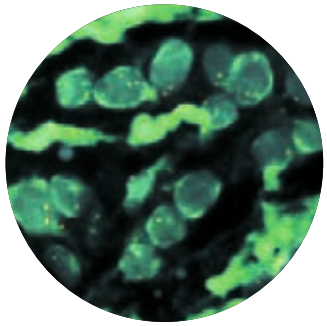
ON MALT (18q21) Break (tissue)

Low grade malignant lymphomas arising from mucosa associated lymphoid tissue (MALT) represent a distinct clinicopathological entity. The three major translocations seen in MALT lymphomas are t(11;18)(q21;q21)/API2-MALT1, t(14;18)(q32;q21)/IGH-MALT1 and t(1;14)(p22;q32)/IGH-BCL10. A break or split probe for MALT (18q21) is best used to analyze translocation of the MALT gene on formalin fixed paraffin embedded tissue for routine clinical diagnosis.

Kreatech has developed this probe for the specific use on cell material (KBI-10608), or for the use on tissue (KBI-10731).

Cat.# KBI-10731 MALT (18q21) Break (tissue)





MALT (18q21) Break tissue probe hybridized to paraffin embedded material (2RG).

Literature:

Morgan et al, 1999, Cancer Res, 59; 6205-6213.
Dierlamm et al, 2000, Blood, 96; 2215-2218.

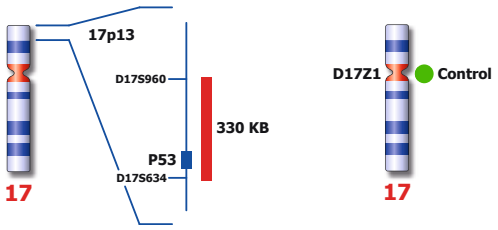
Ordering information	*Color*	*Tests*	*Cat#*
ON MALT (18q21) Break (tissue)	red/green	10	KBI-10731

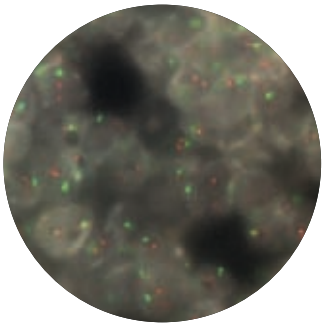
ON p53 (17p13) / SE 17 (tissue)

The p53 tumor suppressor gene at 17p13, has been shown to be implicated in the control of normal cellular proliferation, differentiation, and apoptosis. Allelic loss, usually by deletion, and inactivation of p53 have been reported in numerous tumor types and are associated with poor prognosis in CLL.

The p53 (17p13) specific DNA probe is optimized to detect copy numbers of the p53 gene region at 17p13. The chromosome 17 satellite enumeration probe (SE 17) at D17Z1 is included to facilitate chromosome identification. Kreatech has developed this probe for the specific use on cell material (KBI-10112/KBI-12112), or for the use on tissue (KBI-10738).

Cat.# KBI-10738 p53 (17p13) / SE 17 (tissue)





P53 (17p13) / SE 17 (tissue) probe hybridized to paraffin embedded tissue (2R2G).

Literature:

Amiel A et al, 1997, Cancer Gener.Cytogenet,, 97; 97-100.
Drach J et al, 1998, Blood, 92; 802-809.

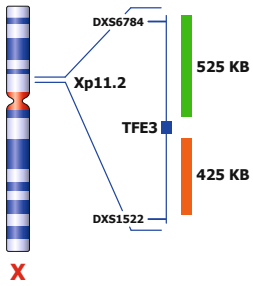
Ordering information	Color	Tests	Cat#
ON p53 (17p13) / SE 17 (tissue)	red/green	10	KBI-10738

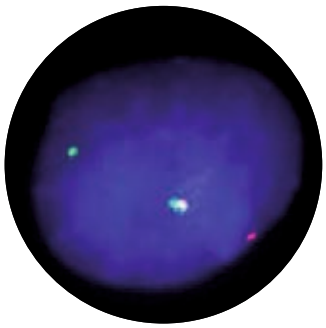
ON TFE3 (Xp11) Break

Abnormalities of Xp11.2 region have often been observed in papillary renal cell carcinomas and are sometimes the sole cytogenetic abnormality present. The transcription factor binding to IGHM enhancer 3 (TFE3) gene, which encodes a member of the helix-loop-helix family of transcription factors, is located in this critical region and can be fused to various other chromosomal regions by translocation. Known fusion partners are NONO (Xq12), PRCC (1q21), SFPQ (1p34), CLTC (17q23) and ASPSCR1 (17q25).

The TFE3 (Xp11) Break probe is optimized to detect translocations involving the TFE3 gene region at Xp11.2 in a dual-color, split assay.

Cat.# KBI-10741 TFE3 (Xp11) Break





TFE3 (Xp11) Break probe hybridized to renal cell carcinoma showing a translocation at Xp11 (1RG1R1G).
Image kindly provided by Dr. Desangles, Paris .

Literature:

Sidhar et al, 1996, Hum Mol Genet, 5; 1333-1338.
Weterman et al., 1996, Proc Natl, Acad Sci, 93; 15294-15298.

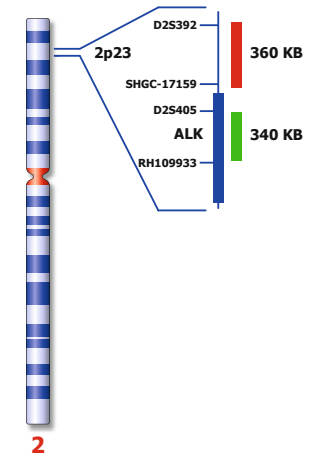
Ordering information	Color	Tests	Cat#
ON TFE3 (Xp11) Break	red/green	10	KBI-10741

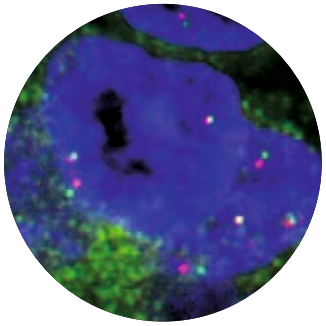
ON ALK (2p23) Break

Translocations of the ALK (anaplastic lymphoma kinase) gene at 2p23 have originally been associated with anaplastic lymphomas, B-cell lymphomas, neuroblastomas and myofibroblastic tumors. To date at least 21 translocation partners have been described, however 80% of the translocations involves the NPM1 gene (5q35). More recently ALK rearrangements have been described in non-small cell lung cancer (NSCLC) cases. Promising results have been obtained with specific anaplastic lymphoma kinase or ALK inhibitors like Crizotinib (Xalkori®) in patients carrying the fusion gene ALK-EML4.

The ALK (2p23) Break probe is optimized to detect translocations involving the ALK gene region at 2p23.

Cat# KBI-10747 ALK (2p23) Break





ALK (2p23) Break probe hybridized to lung adenocarcinoma tissue showing translocation involving the ALK region at 2p23 (1RG1R1G).
Image kindly provided by Prof. B. Terris, Dr. P.A. Just, Hôpital Cochin, Paris.

Literature:

Soda et al., Nature, 2007, 448, 561-566.
Kwak et al, J Clin Oncol., 27(26):4247-53.
Koivunen et al. Clin Cancer Res, 2008, 14, 4275-4283.

Ordering information	*Color*	*Tests*	*Cat#*
ON ALK (2p23) Break	red/green	10	KBI-10747

ONCOLOGY - CHROMOGENIC IN SITU HYBRIDIZATION

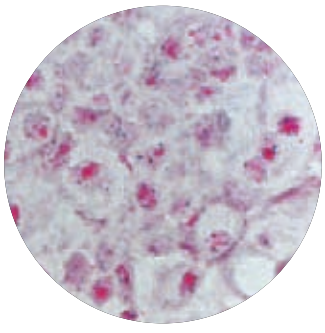
Chromogenic *In Situ* Hybridization (CISH) is increasingly emerging as a viable alternative to FISH and often selected as the method of choice for molecular pathologists for visualizing over-expression of genes involved in tumor development. CISH, like FISH, directly visualizes the number of gene copies present in the nucleus, and it produces a permanent record of the slide that can be interpreted with a regular light microscope in the context of the tumor histopathology.

TwinStar

Our latest product range TwinStar is designed for dual-color CISH enabling the possibility to study ratio of genes in a light microscope, like for the Her-2 gene in relation to the centromeric region of chromosome 17.

Each kit includes the corresponding FISH probes and the specific TwinStar detection module converting both signals into chromogenic signals via a colorimetric assay system.

The TwinStar CISH Detection Kit is a module of all TwinStar assays including all reagents required to perform dual-color CISH. The detection part includes two proprietary substrates converting both fluorescent signals into distinct colorimetric signals, the red fluor is converted into a red signal and the green fluor into a grayish-green signal. TwinStar provides a universal solution capable of transforming all of Kreatech´s dual-color FISH probes into chromogenic signals.

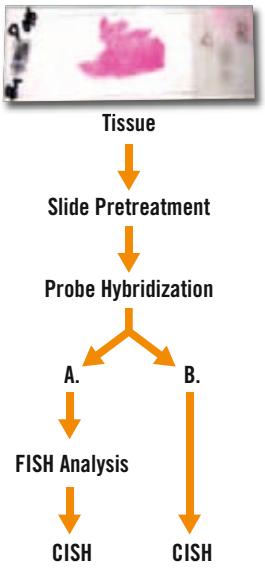


Amplified Her-2/Neu (ERBB2) on a breast cancer specimen visualized with the TwinStar dual color CISH kit.

UniStar

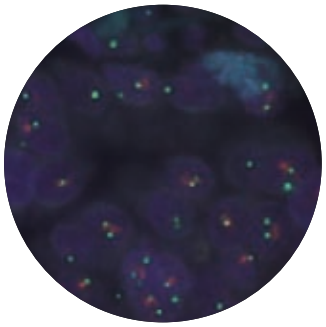
UniStar utilizes a novel assay based on KREATECH's well established POSEIDON™ DNA probes, enabling the clinician to consecutively perform FISH and CISH on the same sample.

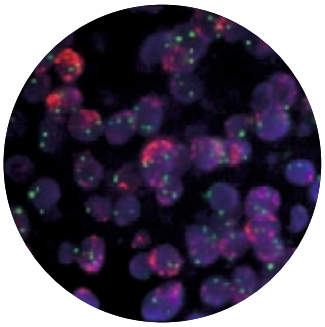
In a first step, the sample is hybridized to specific fluorescent-labeled DNA probes enabling analysis under a fluorescence microscope. Subsequently, the fluorescent signal of the gene of interest can be converted into a chromogenic signal, which can then be analyzed with a regular bright field microscope. Alternatively, FISH can be omitted for direct CISH analysis.

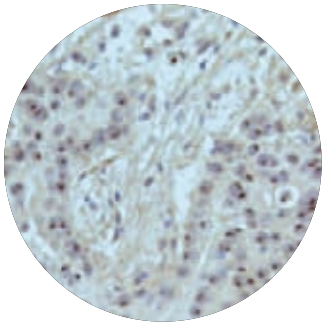


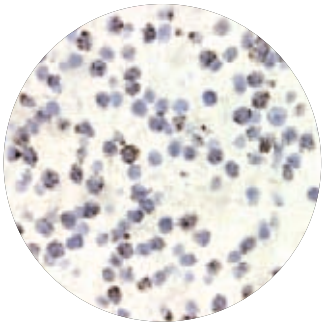
Assay set-up for FISH and CISH analysis with UniStar.

Each of the UniStar kits include the corresponding POSEIDON™ DNA probes for copy number detection of the gene of interest, as well as a control probe for performing FISH in a dual-color assay. In addition, they include a specific detection module converting the signal of the critical probe into a chromogenic single-color signal via a colorimetric assay system.









Example of FISH and CISH performed consecutively on the same slide: breast cancer tissue hybridized with the Her-2/Neu POSEIDON™ fluorescent probe followed by conversion of the red Her-2/Neu signal into a brownish chromogenic signal using the UniStar CISH Detection Kit.

Glioblastoma specimen showing amplified EGFR. The slide was hybridized with the EGFR POSEIDON™ fluorescent probe followed by conversion of the red EGFR signal into a colorimetric signal using the UniStar CISH Detection Kit.
Image kindly provided by Dr. K. Beiske, Oslo University Hospital, Norway.

Product and ordering information

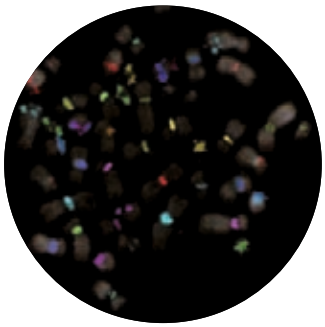
Product	*Description*	*Tests*	*Cat#*
UniStar CISH Detection Kit	UniStar CISH Detection Kit for the use with POSEIDON™ DNA Probes labeled in red	10	KBI-50001
UniStar Her2/neu (17q12)	DNA probes specific for Her-2/Neu and SE 17, UniStar CISH Detection Kit	10	KBI-50701
UniStar EGFR (7p11)	DNA probes specific for EGFR and and SE 7, UniStar CISH Detection Kit	10	KBI-50702
UniStar C-MET (7q31)	DNA probes specific for C-MET and and SE 7, UniStar CISH Detection Kit	10	KBI-50719
TwinStar CISH Detection Kit	For the use with POSEIDON™ DNA probes labeled in red and green	10	KBI-60010
TwinStar Her2/neu (17q12)	DNA probes specific for Her-2/Neu and SE 17, TwinStar CISH Detection Kit	10	KBI-60701
TwinStar EGFR (7p11)	DNA probes specific for EGFR and and SE 7, TwinStar CISH Detection Kit	10	KBI-60702
TwinStar C-MET (7q31)	DNA probes specific for C-MET and and SE 7, TwinStar CISH Detection Kit	10	KBI-60719

PREIMPLANTATION GENETIC SCREENING

FISH is the current gold standard to determine the chromosomal constitution of an embryo. In contrast to karyotyping it can be used on interphase chromosomes, so that it can be applied on polar bodies, blastomeres and other single cell samples. FISH is therefore accepted as a routine method in preimplantation genetic screening (PGS) in determining chromosome aneuploidies prior to implanting an embyro and increases the success rate of an IVF-mediated pregnancy.

MultiStar 24 FISH

MultiStar 24 FISH consists of four DNA probe mixes each hybridizing to six different chromosomes using six different fluorochromes. It can be applied in lymphocytes, sperm and blastomeres.



Metaphase preparation from male lymphocyte cells visualizing all 24 chromosomes.
Image kindly provided by Prof. D. Griffin, University of Kent, United Kingdom.

The fully optimized protocol consists of three 15-30 minutes hybridizations followed by a 6 to 16 hours hybridization. In between the individual hybridizations, the preceding probes are washed off after imaging the results. The morphology of the cell types is retained despite repeated denaturation, hybridization and post hybridization washes. Moreover the entire protocol can be completed within 24 hours, which fits the window for clinical PGS application. This novel method eliminates the bottleneck perceived when using FISH by omitting key chromosomes relevant to implantation failure not covered in a limited panel.

The probes required to provide information for 24 chromosomes comprise four panels each containing 6 chromosome-specific identifier sequences each labelled with a different fluorochrome. The first 3 panels use centromeric sequences (Panel 1: chromosomes 1,3,4,6,7,8; Panel 2: chromosomes 9,10,11,12,17,20 and Panel 3: chromosomes 2,15,16,18,X,Y) . In contrast, Panel 4 used for the final round of hybridization uses unique sequence probes for chromosomes 5,13,14,19,21,22 since centromeric sequences were not available for these chromosomes. A combination of separate probe denaturation for 10 minutes followed by a short co-denaturation between probe and sample is used. Panels 1-3 require short hybridization times (15 minutes) whereas Panel 4 requires a 6 to 16 hours hybridization.

Setup of the different layers

All DNA probes are labeled with Platinum*Bright*™ based on the Universal Linkage System (ULS™), KREATECH´s proprietary non-enzymatic labeling technology capable of linking fluorescent labels or haptens to any nucleic acid of interest.

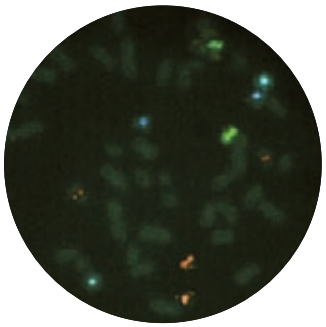
Chromosomes recognized by the different panels:

Color						
Label	Platinum*Bright* 405	Platinum*Bright* 415	Platinum*Bright* 495	Platinum*Bright* 547	Platinum*Bright* 590	Platinum*Bright* 647
Color	Dark Blue	Blue	Green	Light Red	Dark Red	Far Red
Excitation/Emission	410/455	429/470	495/517	547/565	587/612	647/665
MultiStar Panel 1	7	1	6	8	3	4
MultiStar Panel 2	11	9	20	12	10	17
MultiStar Panel 3	18	Y	X	16	2	15
MultiStar Panel 4	19	5	21	22	13	14

PreimpScreen PolB (13,16,18,21,22)

PreimpScreen PolB is designed for determining chromosome copy number in polar bodies.

The first polar body is removed from the unfertilized oocyte, and the second polar body from the zygote, shortly after fertilization. The main advantage of the use of polar bodies in preimplantation genetic screening (PGS) is that they are not necessary for successful fertilization or normal embryonic development, thus ensuring no deleterious effect for the embryo. In some countries, where the legislation bans the selection of preimplantation embryos, polar body analysis is the only possible method to perform PGS. The biopsy and analysis of the first and second polar bodies can be completed before syngamy, which is the moment from which the zygote is considered an embryo and becomes protected by the law.

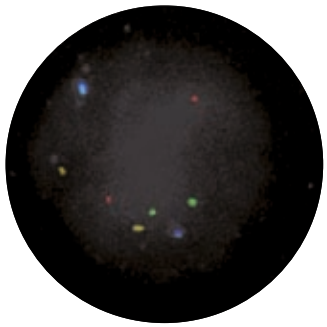


Pseudo color image using PreimpScreen PolB (KBI-40050) on a metaphase spread from lymphocytes showing two signals each of chromosomes 13, 16, 18, 21, and 22, respectively.

PreimpScreen Blas (13,18,21,X,Y)

PreimpScreen Blas is designed for determination of chromosome copy number in blastomeres.

Cleavage-stage biopsy is generally performed the morning of day three post-fertilization, when normally developing embryos reach the eight-cell stage. The biopsy is usually performed on embryos with less than 50% of anucleated fragments and at an 8-cell or later stage of development. The main advantage of cleavage-stage biopsy over polar body (PB) analysis is that the genetic input of both parents can be studied, and therefore currently is the prevalent method when doing in situ hybridizations in preimplantation genetic screening.



Pseudo-color image on a healthy female blastomer using PreimpScreen Blas (13,18,21,X,Y) FISH panel, KBI-40051.
Image kindly provided by Prof. D. Griffin, University of Kent, United Kingdom.

Literature:
Iaonnou D et al, 2012, Chromosome Res, 20:447-60.
Iaonnou D et al, 2011, Mol and Cel Probes, 25:199-205.

Product and ordering information

Product	*Description*	*Tests*	*Cat#*
PreimpScreen PolB (13,16,18,21,22)	Five-color FISH-mix consisting of DNA probes specific for chromosomes 13, 16, 18, 21, and 22	20	KBI-40050
PreimpScreen Blas (13,18,21,X,Y)	Five-color FISH-mix consisting of DNA probes specific for chromosomes 13, 18, 21, X, and Y	20	KBI-40051
MultiStar 24 FISH	FISH probe panel for visualizing all 24 chromosomes (including the four panels KBI-40061, KBI-40062, KBI-40063, and KBI-40064)	10	KBI-40060
MultiStar FISH Panel 1	FISH panel of centromeric probes for chromosomes 1, 3, 4, 6, 7, and 8	10	KBI-40061
MultiStar FISH Panel 2	FISH panel of centromeric probes for chromosomes 9, 10, 11, 12, 17, and 20	10	KBI-40062
MultiStar FISH Panel 3	FISH panel of centromeric probes for chromosomes 2, 15, 16, 18, X, and Y	10	KBI-40063
MultiStar FISH Panel 4	FISH panel of unique sequence probes for chromosomes 5, 13, 14, 19, 21, and 22	10	KBI-40064

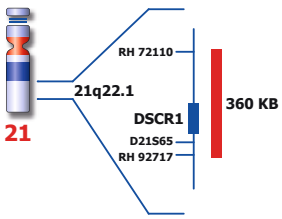
PRENATAL DNA PROBES

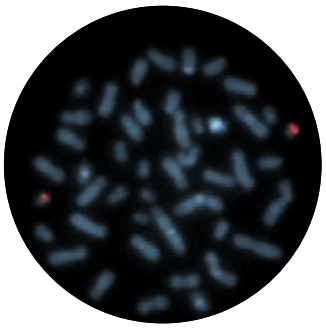
Prenatal cytogenetic analysis requires the isolation of metaphase chromosomes and takes 7-14 days for the final results. This waiting period tends to cause psychological distress for pregnant women and their families. Aneuploidies of 5 chromosomes (13, 18, 21, X, Y) account for 95% of the chromosomal aberrations that cause infants born with defects. Fluorescent labeled DNA probes of the 13, 18, 21, X, Y chromosomes can be used on uncultured cells obtained directly from amniotic fluid. The FISH rapid technique allows to reliably detect numerical aberrations for these chromosomes. While not all chromosome abnormalities can be identified simply by counting specific chromosomes within a cell, the majority of the most common abnormalities of chromosome number, including Down syndrome (trisomy 21), trisomy 18, trisomy 13, Klinefelter syndrome (47,XXY), triple-X syndrome (47,XXX), Turner syndrome (45,X) and 47,XYY can be reliably determined. The FISH analysis does not detect structural chromosome abnormalities, mosaicism, and other numerical chromosome abnormalities (excluding X, Y, 13, 18, and 21). In addition, false-positive or negative results, as well as maternal cell contamination, have been demonstrated in prenatal FISH analysis. It is recommended (e.g. American College of Medical Genetics) that irreversible therapeutic action should not be initiated on the basis of FISH results alone.

Trisomy 21 – Down Syndrome

Down syndrome is caused by an extra chromosome 21. It is the most common single cause of human birth defects, with an occurrence in 1 out of every 660 births. Congenital heart defects are frequently present in Down syndrome children. The normal life span mainly is shortened in Down syndrome by congenital heart disease and by increased incidence of acute leukemia. Mental retardation is variable, and usually moderate. Some adults live independently and are accomplished individuals. The chromosome 21 specific region probe is optimized to detect copy numbers of chromosome 21 at 21q22.1 on uncultured amniotic cells. In all PN combinations the 21q specific DNA probe is direct-labeled in red with Platinum*Bright*550.

Cat.# KBI-40002 PN 21 (21q22)





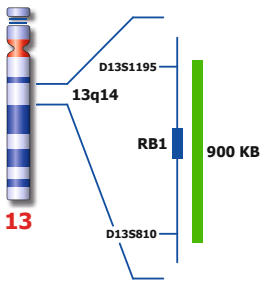
PN 21 (21q22) probe hybridized to a normal metaphase (2R).

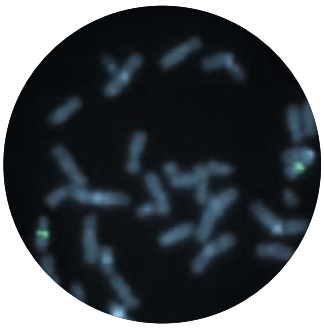
Trisomy 13 – Patau Syndrome

Trisomy 13, also called Patau syndrome, is a chromosomal condition that is associated with severe mental retardation and certain physical abnormalities. Affected individuals rarely live past infancy because of the life-threatening medical problems associated with this condition. Trisomy 13 affects approximately 1 in 10,000 newborns. The risk of having a child with trisomy 13 increases as a woman gets older.

The chromosome 13 specific region probe is optimized to detect copy numbers of chromosome 13 at 13q14.2 on uncultered amniotic cells. In all PN combinations the 13q14 specific DNA probe is direct-labeled in green with Platinum*Bright*495.

Cat.# KBI-40001 PN 13 (13q14)



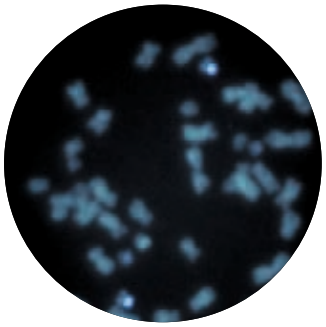


PN 13 (13q14) probe hybridized to a normal metaphase (2G).

Trisomy 18 – Edward Syndrome

Trisomy 18 is caused by an extra chromosome 18 and usually consists of mental retardation, small birth size, and many developmental anomalies, including severe microcephaly, prominent occiput, low-set malformed ears, and a characteristic pinched facial appearance. Trisomy 18 occurs 1 in 6000 live births, but spontaneous abortions are common. More than 95% of affected children have complete trisomy 18. The extra chromosome is almost always maternally derived, and advanced maternal age increases risk.

Cat.# KBI-20018-B SE 18 (D18Z1)

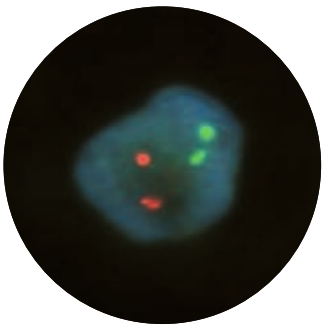


SE 18 (D18Z1) probe hybridized to a normal metaphase showing two blue signals (2B).

The chromosome 18 specific Satellite Enumeration (SE 18) probe (D18Z1) is optimized to detect copy numbers of chromosome 18 at 18p11-18q11 on uncultured amniotic cells. In all PN combinations the 18 SE centromeric DNA probe is offered direct-labeled in blue with Platinum*Bright*415.

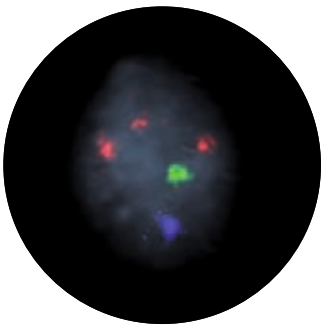
Other combinations

Cat.# KBI-40003



PN 13 (13q14) / 21 (21q22) probe hybridized to a normal interphase (2R2G).

Cat.# KBI-40008



Ploidyscreen (21, X, Y) showing trisomy 21.
Material kindly provided by Prof. Wegner, Berlin.

Sex Chromosome Abnormalities

Chromosomal abnormalities involving the X and Y chromosome (sex chromosomes) are slightly less common than autosomal abnormalities and are usually much less severe in their effects. The high frequency of people with sex chromosome aberrations is partly due to the fact that they are rarely lethal conditions.

- **Turner syndrome** occurs when females inherit only one X chromosome – their genotype is X0.
- **Metafemales or triple-X females**, inherit three X chromosomes – their genotype is XXX or more rarely XXXX or XXXXX.
- **Klinefelter syndrome** males inherit one or more extra X chromosomes – their genotype is XXY or more rarely XXXY, XXXXY, or XY/XXY mosaic.
- **XYY syndrome** males inherit an extra Y chromosome – their genotype is XYY.

The chromosome X specific SE probe (DXZ1) is optimized to detect copy numbers of chromosome X at Xp11-Xq11 on uncultured amniotic cells. The chromosome Y specific SE probe (DYZ3) is optimized to detect copy numbers of chromosome Y at Yp11-Yq11 on uncultured amniotic cells. In all Prenatal Probes combinations the X SE centromeric DNA probe is offered direct-labeled in green with Platinum*Bright*495.

Technical information

In most Prenatal Probes combinations the Y SE centromeric DNA probe is offered direct-labeled in red with Platinum*Bright*550, except for the KBI-40008 where the Y SE is labeled in blue with Platinum*Bright*415. All prenatal probes are in a Ready-to-Use for more convenience. This format still allows adding of a SE 18 probe.

Product and ordering information

Description	*Color*	*Tests*	*Cat#*
PN 13 (13q14)	green	10	KBI-40001
PN 21 (21q22)	red	10	KBI-40002
PN 13 (13q14) / 21 (21q22)	green/red	10	KBI-40003
SE 18 (D18Z1) 5x conc	blue	10	KBI-20018-B
SE X (DXZ1) / SE Y (DYZ3)	green/red	10	KBI-20030
SE 7 (D7Z1) / SE 8 (D8Z1)	red/green	10	KBI-20031
SE (X,Y,18)	green/red/blue	10	KBI-20032
PrenatScreen (13/21, X/Y18)	green/red/blue	10	KBI-40005
PrenatScreen (13/21, X/Y18)	green/red/blue	30	KBI-40006
PrenatScreen (13/21, X/Y18)	green/red/blue	50	KBI-40007
PloidyScreen (21, X, Y)	red/green/blue	20	KBI-40008

MICRODELETION DNA PROBES

Microdeletion syndromes are usually caused by a chromosomal deletion spanning one or several genes that are too small to be detected under the microscope using conventional cytogenetic methods. Fluorescence *In Situ* Hybridization (FISH) can be employed to identify such deletions and therefore becomes the method of choice for diagnosing microdeletion syndromes.

The REPEAT-FREE™ POSEIDON™ Microdeletion Probes are direct labeled, Ready-to-Use in hybridization buffer and available in a 5 or a 10 test kit.

Table of Contents

DiGeorge / Velocardiofacial Syndrome (VCFS)

Microdeletion of chromosome 22 accounts for more than 90% of cases of DiGeorge anomaly which has an incidence of 1 in 4000 live births. Deletions of chromosome 22q11.2 are found in the vast majority of patients with DiGeorge anomaly and VCFS.

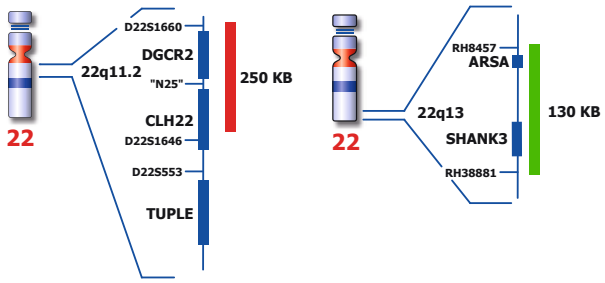
Most deletions are *de novo*, with 10% or less inherited from an affected parent. All probes that are currently in use to detect deletions in DiGeorge and VCFS are located within the described minimal critical region of 1.5 Mb.

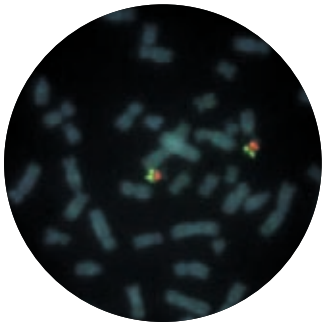
MD DiGeorge “N25” (22q11) / 22q13 (SHANK3)

The DiGeorge “N25” probe was the first commercial microdeletion probe for chromosome 22q and detects the locus D22S75. This marker is located between DGCR2 and CLH22 (Clathrin). Both genes have been extensively investigated and their role in DiGeorge syndrome is well established.

The DiGeorge ”N25” region probe covers the marker “N25” (D22S75) and adjacent region of CLH22 (Clathrin gene region) and DGCR2 (DiGeorge critical region gene 2). The SHANK3 probe at 22q13 is serving as internal control.

Cat.# KBI-40102 MD DiGeorge “N25” (22q11) / 22q13 (SHANK3)





MD DiGeorge "N25" (22q11) / 22q13 (SHANK3) probe hybridized to a normal metaphase (2R2G).

Literature:

Sirotkin et al, 1996, Hum Mol Genet, 5: 617-624.
Holmes et al, 1997, Hum Mol Genet, 6: 357-367.
Wilson, et al, 2003, J Med Genet 40; 575-584.
Luciani, et al, 2003, J Med Genet 40; 690-696.

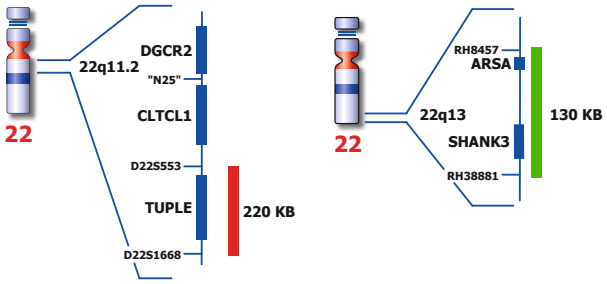
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD DiGeorge “N25” (22q11) / 22q13 (SHANK3)	N25	10	KBI-40102

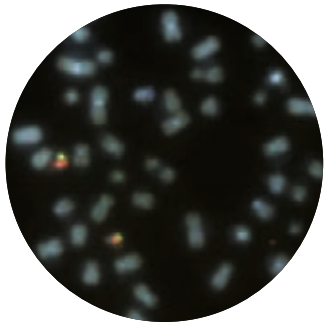
MD DiGeorge “TUPLE” (22q11) / 22q13 (SHANK3)

The DiGeorge ”Tuple” probe targets a putative transcriptional regulator (TUPLE1 or HIRA, HIR histone cell cycle regulation defective homolog A) which also has been identified to lie within the commonly deleted region DiGeorge syndrome. This probe is located distally to the “N25” probe. The DiGeorge “Tuple” region probe is optimized to detect copy numbers of the Tuple (Hira) gene region at 22q11.2.

The SHANK3 probe at 22q13 is serving as internal control.

Cat.# KBI-40103 DiGeorge “Tuple” (22q11) / 22q13 (SHANK3)





MD DiGeorge "Tuple" (22q11) / 22q13 (SHANK3) probe hybridized to a normal metaphase (2R2G).

Literature:

Lorain at al, 1996, Genome Res, 6: 43-50.

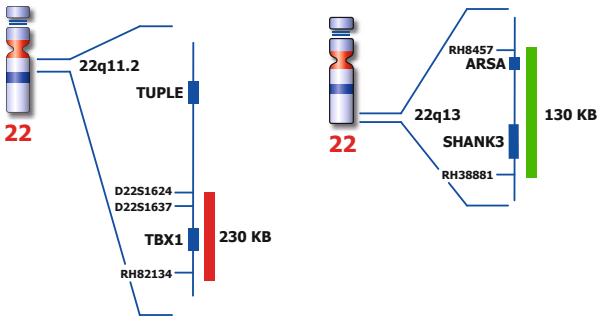
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD DiGeorge Tuple (22q11) / 22q13 (SHANK3)	TUPLE	10	KBI-40103

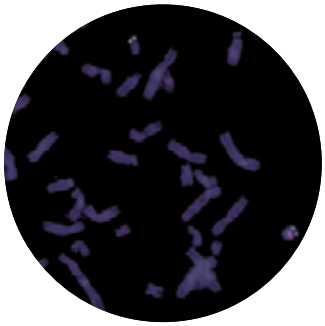
MD DiGeorge T-Box1 (22q11) / 22q13 (SHANK3)

The 22q11 deletion in DiGeorge syndrome/VCFS is characterized by defects in the derivatives of the pharyngeal apparatus. TBX1, a member of the T-box transcription factor family, is required for normal development of the pharyngeal arch arteries. Haploinsufficiency of TBX1 has been demonstrated to be sufficient to generate at least one important component of the DiGeorge syndrome phenotype in mice. The TBX1 is also located within the minimal critical DiGeorge region in humans.

The DiGeorge TBX1 region probe is optimized to detect copy numbers of the TBX1 gene region at 22q11.2. The subtelomeric (ST) 22qter DNA probe is included as control probe. The SHANK3 probe at 22q13 is serving as internal control.

Cat.# KBI-40104 MD DiGeorge T-box1 (22q11) / 22q13 (SHANK3)





MD DiGeorge T-box1 (22q11) / 22q13 (SHANK3) probe hybridized to DiGeorge patient material showing a deletion of the TBX1 gene region at 22q11 (1R2G).
Image kindly provided by Dr. F. Girard-Lemaire, Service de Cytogénétique (Dr. Flori), CHU Strasbourg.

Literature:

Lindsay et al, 2001, Nature, 410: 97-101.
Merscher et al, 2001, Cell, 104: 619-629.
Paylor et al, 2006, PNAS, 103: 7729-7734.

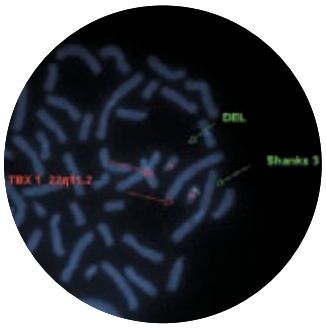
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD DiGeorge T-box1 (22q11) / 22q13 (SHANK3)	TBX1	10	KBI-40104

Phelan-McDermid Syndrome

The 22q13 deletion syndrome (or Phelan-McDermid syndrome) is characterized by moderate to profound mental retardation, delay/absence of expressive speech, hypotonia, normal to accelerated growth, and mild dysmorphic features. A terminal deletion including the SHANK3 gene region has been identified for this syndrome.

MD DiGeorge (22q11) / 22q13 (SHANK3)

The 22q13 DNA probe is optimized to detect copy numbers of the SHANK3 gene region at 22q13. The DiGeorge region probe at 22q11 is serving as internal control.



MD DiGeorge T-box1 (22q11) / 22q13 (SHANK3) probe hybridized to patient material showing a deletion of the SHANK3 region at 22q13 (2R1G).

Literature:

Wilson, et al, 2003, J Med Genet 40; 575-584.
Luciani, et al, 2003, J Med Genet 40; 690-696.

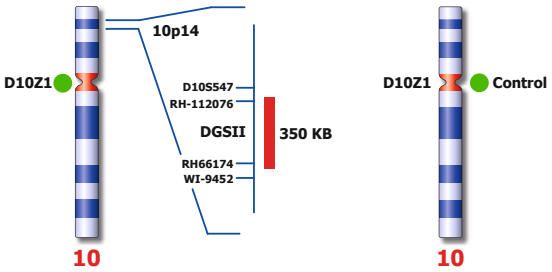
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD DiGeorge "N25" (22q11) / 22q13 (SHANK3)	N25	10	KBI-40102
MD DiGeorge Tuple (22q11) / 22q13 (SHANK3)	TUPLE	10	KBI-40103
MD DiGeorge T-box1 (22q11) / 22q13 (SHANK3)	TBX1	10	KBI-40104

MD DiGeorge II (10p14) / SE 10

DiGeorge and VCFS present many clinical problems and are frequently associated with deletions within 22q11.2 (see previous probes), but a number of cases have no detectable molecular defect of this region. A number of single case reports with deletions of 10p suggest genetic heterogeneity of DiGeorge syndrome. FISH analysis demonstrates that these patients have overlapping deletions at the 10p13/10p14 boundary. The shortest region of deletion overlap (SRO) has been identified in a 1 cM interval including makers D10S547 and D10S585.

The DiGeorge II region probe is optimized to detect copy numbers of the DGSII at 10p14. The chromosome 10 satellite enumeration (SE 10) probe at D10Z1 is included to facilitate chromosome identification.

Cat.# KBI-40105 MD DiGeorge II (10p14) / SE 10



MD DiGeorge II(10p14) / SE 10 probe hybridized to DiGeorge II patient material showing a deletion of the DGSII region at 10p14 (1R2G).
Imaqe kindly provided by Azzedine Aboura, Hôpital Robert Debré Paris.

Literature:

Monaco et al, 1991, Am J Med Genet, 39: 215-216.
Schuffenhauer et al, 1998, Eur J Hum Genet, 6: 213-225.

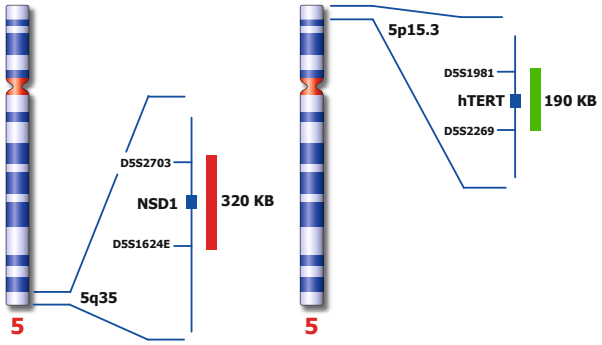
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD DiGeorge II (10p14) / SE 10	10p-	10	KBI-40105

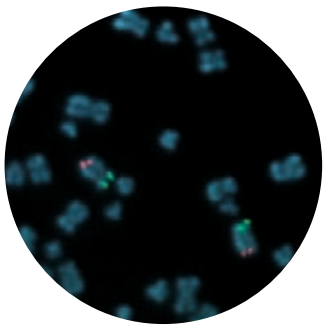
MD NSD1 (5q35) / hTERT (5p15)

NSD1 microdeletions (chromosome 5q35) are the major cause of Sotos syndrome, and occur in some cases of Weaver syndrome. Sotos is a childhood overgrowth characterized by distinctive craniofacial features, advanced bone age, and mental retardation. Weaver syndrome is characterized by the same criteria but has its own specific facial characteristics.
Sotos syndrome is inherited in an autosomal dominant manner. While 50% of Sotos patients in Asia are showing a chromosomal microdeletion, only 9% deletion cases are observed in the affected European population.

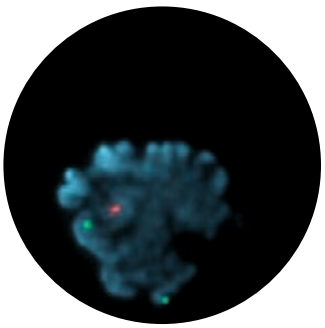
The NSD1 (5q35) region probe is optimized to detect copy numbers of the NSD1 gene region at 5q35.2. The hTERT region specific DNA probe at 5p15 is included as control probe.

Cat.# KBI-40113 NSD1 (5q35) / hTERT (5p15)





NSD1 (5q35) / hTERT (5p15) probe hybridized to a normal metaphase (2R2G).



NSD1 (5q35) / hTERT (5p15) probe hybridized to patient material showing a microdeletion of the NSD1 gene region at 5q35 (1R2G).

Literature:
Douglas et al, 2003, Am. J. Hum. Genet. 72; 132-143.
Rio et al, 2003, J. Med. Genet. 40; 436-440.

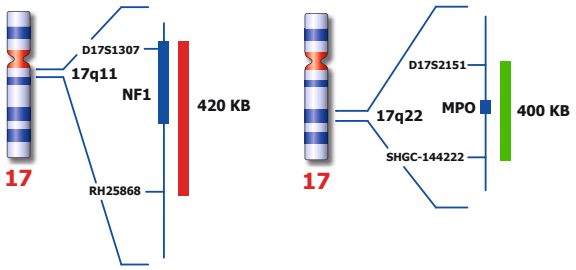
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD NSD1 (5q35) / hTERT (5p15)	NSD1	10	KBI-40113

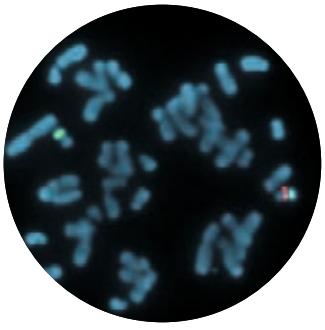
MD NF1 (17q11) / MPO (17q22)

NF1, or von Recklinghausen disease, is one of the most common hereditary neurocutaneous disorders in humans and one of the most common single gene syndromes. Clinically, NF1 is characterized by café-au-lait spots, freckling, skin neurofibroma, plexiform neurofibroma, bone defects, Lisch nodules and tumors of the central nervous system. The responsible gene, NF1 (neurofibromin), was identified on chromosome 17q11. Whole NF1 gene deletions occur in 4%-5% of individuals with NF1 and can be detected by FISH analysis.

The NF1 (17q11) region probe is optimized to detect copy numbers of the NF1 gene region at 17q11.2.
The MPO region specific DNA probe at 17q22 is included as control probe.

Cat.# KBI-40114 NF1 (17q11) / MPO (17q22)





NF1 (17q11) / MPO (17q22) probe hybridized to patient material showing a deletion of NF1 gene region at 17q11 (1R2G).

Literature:
Riva P et al, 2000, Am.J.Hum.Genet. 66; 100-109.
Dorschner et al, 2000, Hum.Mol.Genet. 9; 35-46.

Ordering information	*Gene Region*	*Tests*	*Cat#*
MD NF1 (17q11) / MPO (17q22)	NF1	10	KBI-40114

Prader-Willi/Angelman Syndrome

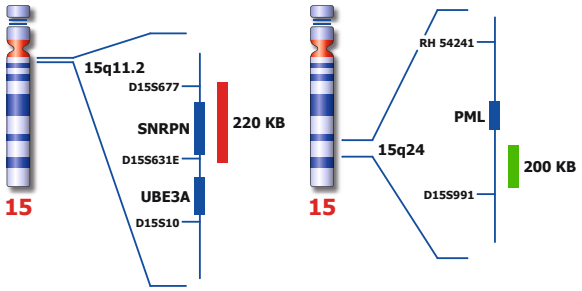
Prader-Willi syndrome (PWS) and Angelman syndrome (AS) are clinically distinct complex disorders mapped to chromosome 15q11-q13. They both have characteristic neurologic, developmental, and behavioral phenotypes plus other structural and functional abnormalities. However, the cognitive and neurologic impairment is more severe in AS, including seizures and ataxia. The behavioral and endocrine disorders are more severe in PWS, including obsessive-compulsive symptoms and hypothalamic insufficiency. Both disorders can result from microdeletion, uniparental disomy, or an imprinting center defect in 15q11-q13.

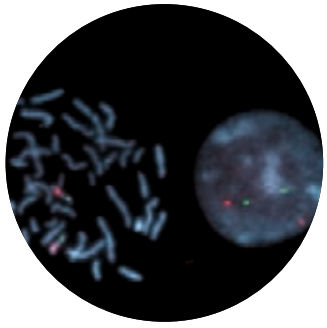
MD Prader-Willi SNRPN (15q11) / PML (15q24)

Prader-Willi syndrome (PWS) is a clinically distinct disorder including diminished fetal activity, obesity, hypotonia, mental retardation, short stature, hypogonadotropic hypogonadism, strabismus, and small hands and feet.

Approximately 70% of cases of PWS arise from paternal deletion of the 15q11-q13 region including the gene SNRPN (small nuclear ribonucleoprotein polypeptide N). The PWS SNRPN region probe is optimized to detect copy numbers of the SNRPN gene region at 15q11. The PML (promyelocytic leukemia) gene specific DNA probe at 15q24 is included as control probe.

Cat.# KBI-40109 Prader-Willi SNRPN (15q11) / PML (15q24)





Prader-Willi SNRPN (15q11) / PML (15q24) probe hybridized to a normal interphase/metaphase (2R2G).

Literature:

Knoll et al, 1989, Am J Med Genet, 32: 285-290.
Ozcelik et al, 1992, Nat Genet, 2: 265-269.

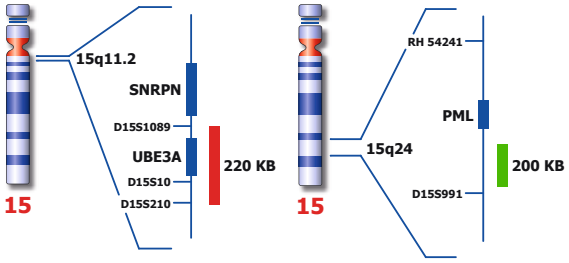
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD Prader-Willi SNRP (15q11) PML (15q24)	SNRPN	10	KBI-40109

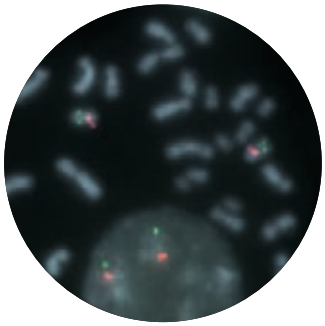
MD Angelman UBE3A (15q11) / PML (15q24)

Angelman syndrome (AS) is characterized by severe developmental delay or mental retardation, severe speech impairment, gait ataxia and/or tremulousness of the limbs, and an unique behavior with an inappropriate happy demeanor that includes frequent laughing, smiling, and excitability. In addition, microcephaly and seizures are common. AS is caused by absence of a maternal contribution to the imprinted region on chromosome 15q11-q13 including the UBE3A gene.

The AS UBE3A region probe is optimized to detect copy numbers of the UBE3A gene region at 15q11. The PML (promyelocytic leukemia) gene specific DNA probe at 15q24 is included as control probe.

Cat.# KBI-40110 Angelman UBE3A (15q11) / PML (15q24)





Angelman UBE3A (15q11) / PML (15q24) probe hybridized to a normal interphase/metaphase (2R2G).

Literature:
Matsuura et al, 1997, Nat Genet, 15: 74-77.
Burger et al, 2002, Am J Med Genet, 111: 233-237.

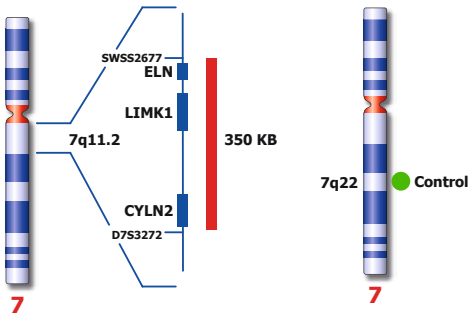
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD Angelman UBE3A (15q11) / PML (15q24)	UBE3A	10	KBI-40110

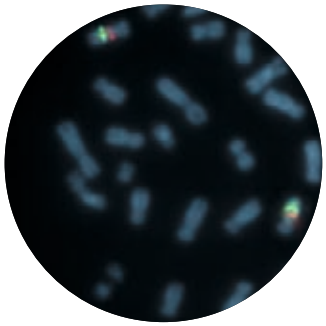
MD Williams-Beuren ELN (7q11) / 7q22

Williams-Beuren syndrome (WS) is characterized by cardiovascular disease, distinctive facial features, connective tissue abnormalities, mental retardation and endocrine abnormalities. Over 99% of individuals with the clinical diagnosis of WS have this contiguous gene deletion, that encompasses the elastin (ELN) gene region including ELN, LIMK1, and the D7S613 locus.

The Williams-Beuren region probe is optimized to detect copy numbers of the ELN gene region at 7q11. The 7q22 region specific DNA probe at 7q22 is included as control probe.

Cat.# KBI-40111 Williams-Beuren ELN (7q11) / 7q22





Williams-Beuren ELN (7q11) / 7q22 probe hybridized to a normal metaphase (2RG).

Literature:
Ewart, et al, 1993, Nat Genet, 5: 11-16.
Botta et al, 1999, J Med Genet, 36: 478-480.

Ordering information	*Gene Region*	*Tests*	*Cat#*
MD Williams-Beuren ELN (7q11) / 7q22	ELN	10	KBI-40111

MD Miller-Dieker LIS (17p13) / Smith-Magenis RAI (17p11)

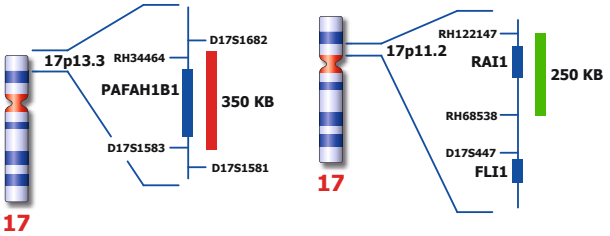
Miller-Dieker Syndrome (MDS) is characterized by classical lissencephaly and distinct facial features. The lissencephaly represents the severe end of the spectrum with generalized agyria or agyria with some frontal pachygyria. Submicroscopic deletions of 17p13.3 including the LIS1 (now called PAFAH1B1, platelet-activating factor acetylhydrolase) gene are found in almost 100% of patients.

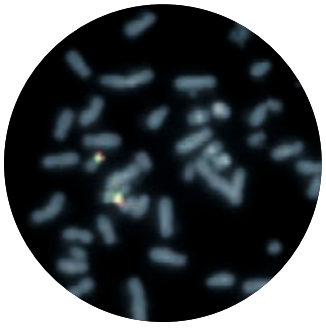
The Miller-Dieker region probe is optimized to detect copy numbers of the PAFAH1B1 gene (LIS1) region at 17p13.3. The Smith-Magenis RAI1 region probe at 17p11.2 is serving as internal control.

Smith-Magenis Syndrome (SMS) is characterized by distinctive facial features that progress with age, developmental delay, cognitive impairment, and behavioral abnormalities. Molecular cytogenetic analysis by FISH using a DNA probe specific for the SMS critical region is recommended in cases of submicroscopic deletions and/or to resolve equivocal cases. RAI1 is the only gene known to account for a majority of features in SMS. All 17p11.2 deletions associated with SMS include a deletion of RAI1.

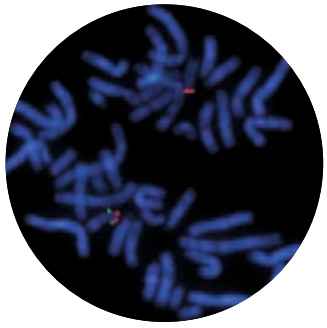
The Smith-Magenis region probe is optimized to detect copy numbers of the RAI1 gene region involved in Smith-Magenis syndrome at 17p11.2. The Miller-Dieker LIS1 probe at 17p13.3 is serving as internal control.

Cat.# KBI-40101 Miller-Dieker LIS (17p13) / Smith-Magenis RAI (17p11)





Miller-Dieker LIS (17p13) / Smith-Magenis RAI (17p11) probe hybridized to a normal metaphase (2RG).



Miller-Dieker LIS (17p13) / Smith-Magenis RAI (17p11) probe hybridized to Smith-Magenis patient material showing a deletion of the RAI1 gene region at 17p11 (2R1G).
Image kindly provided by Prof. Jauch, Heidelberg.

Literature:
Kuwano et al, 1991, Am J Hum Genet, 49: 707-714.
Cardoso et al, 2003, Am J Hum Genet, 72: 918-930.

Literature:
Smith et al, 1986, Am J Med Genet, 24: 393-414.
Greenberg et al, 1991, Am J Med Genet, 49: 1207-1218.
Vlangos et al, 2005, Am J Med Genet, 132: 278-282.

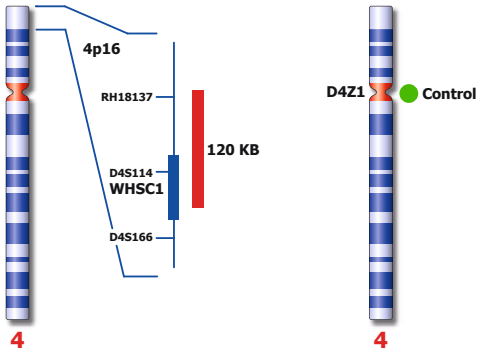
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD Miller-Dieker LIS (17p13) / Smith-Magenis RAI (17p11)	LIS1/RAI1	10	KBI-40101

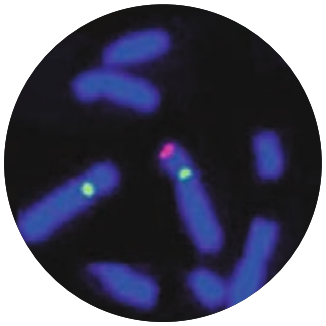
MD Wolf-Hirschhorn WHSC1 (4p16)

Wolf-Hirschhorn syndrome (WHS) affected individuals have prenatal-onset growth deficiency followed by postnatal growth retardation and hypotonia with muscle under-development. Developmental delay/mental retardation of variable degree is present in all. FISH analysis using a WHSC1 specific probe for chromosomal locus 4p16.3 detects more than 95% of deletions in WHS.

The Wolf-Hirschhorn region probe is optimized to detect copy numbers of the Wolf-Hirschhorn critical region at 4p16. The chromosome 4 satellite enumeration (SE 4) probe at D4Z1 is included to facilitate chromosome identification.

Cat.# KBI-40107 Wolf-Hirschhorn WHSC1 (4p16) / SE 4





Wolf-Hirschhorn WHSC1 (4p16) / SE 4 probe hybridized to Wolf-Hirschhorn patient material showing a deletion of the WHSC1 gene region at 4p16 (1R2G). Image kindly provided by Prof. Zollino, Rome.

Literature:
Gandelman et al, 1992, Am J Hum Genet, 51: 571-578.
Wright et al, 1997, Hum Mol Genet, 6: 317-324.

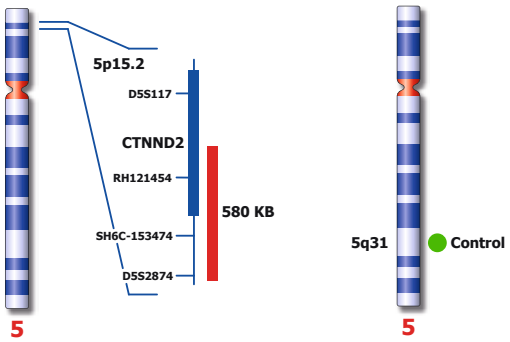
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD Wolf-Hirschhorn WHSC1 (4p16) / SE 4	WHSC1	10	KBI-40107

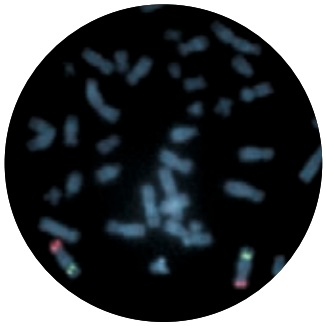
MD Cri-Du-Chat CTNND (5p15) / 5q31

Cri-Du-Chat syndrome is an autosomal deletion syndrome caused by a partial deletion of chromosome 5p. It is characterized by a distinctive, high-pitched, catlike cry in infancy with growth failure, microcephaly, facial abnormalities, and mental retardation throughout life. Loss of a small region in band 5p15.2 (Cri-Du-Chat critical region) correlates with all the clinical features of the syndrome with the exception of the catlike cry, which maps to band 5p15.3 (catlike cry critical region).

The Cri-Du-Chat region probe is optimized to detect copy numbers at the CTNND2 gene region in the Cri-Du-Chat critical region at 5p15.2. The 5q31 specific DNA probe is included as control probe.

Cat.# KBI-40106 Cri-Du-Chat CTNND (5p15) / 5q31





Cri-Du-Chat CTNND (5p15) / 5q31 probe hybridized to a normal metaphase (2R2G).

Literature:
Overhauser et al, 1994, Hum Mol Genet, 3: 247-252.
Gersh et al, 1997, Cytogenet Cell Genet, 77: 246-251.

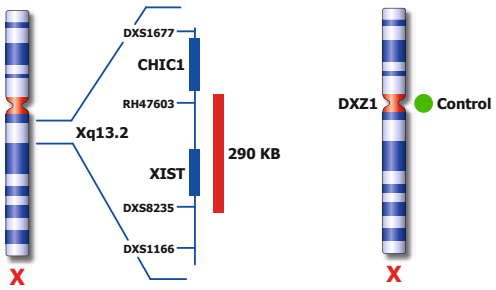
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD Cri-Du-Chat CTNND (5p15) / 5q31	5p-	10	KBI-40106

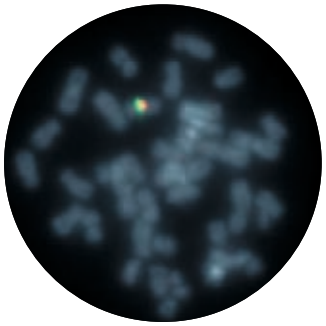
MD X-Inactivation XIST (Xq13) / SE X

The XIST locus is expressed only from the inactive X chromosome, resides at the putative X inactivation centre, and is considered a prime player in the initiation of mammalian X dosage compensation. The severe phenotype of human females whose karyotype includes tiny ring X chromosomes has been attributed to the inability of the small ring X chromosome to inactivate. Many of the ring chromosomes lack the XIST locus, consistent with XIST being necessary for cis inactivation.

The XIST specific DNA probe is optimized to detect copy numbers of the XIST region at Xq13. The chromosome X satellite enumeration (SE X) probe at DXZ1 is added to facilitate chromosome identification.

Cat.# KBI-40108 X-Inactivation XIST (Xq13) / SE X





X-Inactivation XIST (Xq13) / SE X probe hybridized to a male metaphase (1R1G).

Literature:

Migeon et al, 1993, PNAS, 90: 12025-12029.
Jani et al, 1995, Genomics, 27: 182-188.

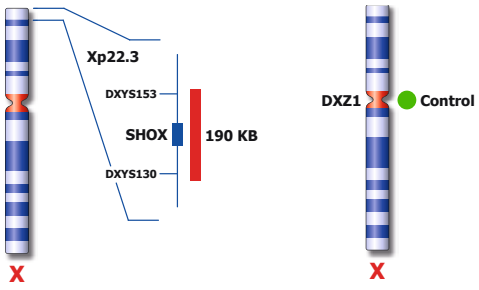
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD X-Inactivation XIST (Xq13) / SE X	XIST	10	KBI-40108

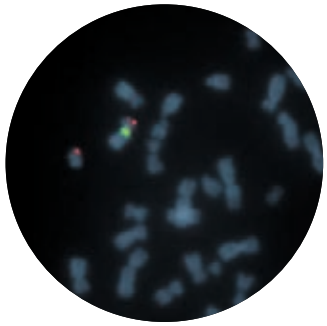
MD Short Stature (Xp22) / SE X

Individuals with SHOX-related short stature have disproportionate short stature and/or wrist abnormalities consistent with those described in Madelung deformity. The SHOX genes located on the pseudoautosomal regions of the X and Y chromosomes are the only genes known to be associated with SHOX-related haploinsufficiency.

The SHOX region probe is optimized to detect copy numbers of the SHOX gene region at Xp22. The chromosome X satellite enumeration (SE X) probe at DXZ1 is added to facilitate chromosome identification.

Cat.# KBI-40112 Short stature (Xp22) / SE X





Short stature (Xp22) / SE X probe hybridized to a male metaphase (2R1G).

Literature:

Rao et al, 1997, Hum Genet, 100: 236-239.
Morizio et al, 2003, Am J Med Genet, 119: 293-296.

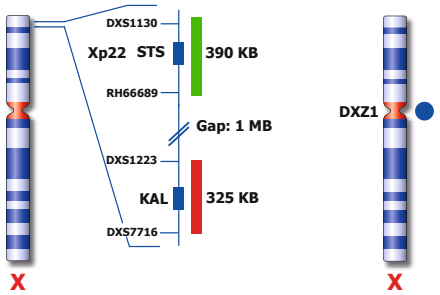
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD Short Stature (Xp22) / SE X	SHOX	10	KBI-40112

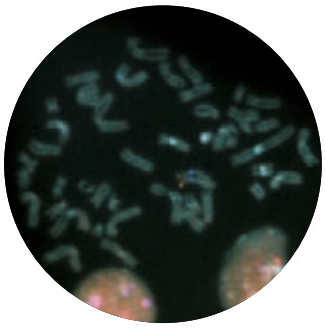
MD STS (Xp22) / KAL (Xp22) / SE X TC

STS (Steroid Sulfatase) disease is a chromosome X-linked disorder associated with a microdeletion of the gene within the Xp22.3 region. Deletion of the steroid sulfatase gene has been detected in individuals with recessive X-linked ichtyosis, the disease been considered one of the most frequent human enzyme deficient disorders. KAL1 (Kallmann syndrome interval gene-1) maps to the Kallmann syndrome critical region on the distal short arm of the human X chromosome. Individuals with Kallmann syndrome suffers from hypogonadotropic hypogonadism and anosmia, with clinical features of variable phenotype. It affects approximately 1 in 8000 males and 1 in 40000 females.

The STS (Xp22) region probe is optimized to detect copy numbers of the STS gene region at Xp22. The KAL (Xp 22) region probe is optimized to detect copy numbers of the KAL gene region at Xp22. The Chromosome X Satellite Enumeration (SE X) probe at DXZ1 is included to facilitate chromosome identification.

Cat.# KBI-40115 STS (Xp22) / KAL (Xp22) / SE X TC





STS (Xp22) / KAL (Xp22) / SE X TC probe hybridized to male patient material showing a deletion of the STS gene region (1R1B).
Material kindly provided by Necker hospital, Paris.

Literature:

Alper in et al, 1997, J. Biol. Chem 272; 20756-20763.
Meroni et al, 1996, Hum. Mol. Genet. 5; 423-431.

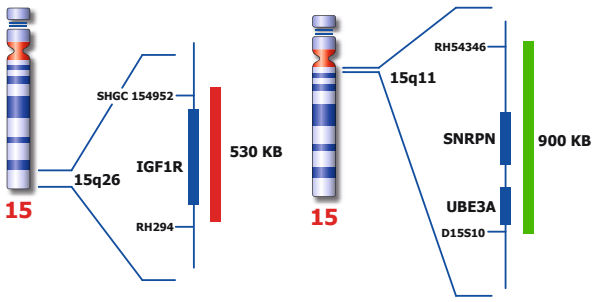
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD STS (Xp22) / KAL (Xp22) / SE X TC	STS/KAL	10	KBI-40115

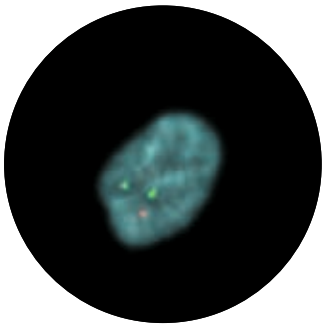
MD IGF1R (15q26) / 15q11

Congenital diaphragmatic hernia (CDH) is a severe, life-threatening, congenital anomaly characterized by variable defects in the diaphragm, pulmonary hypoplasia, and postnatal pulmonary hypertension. Deletion of the IGF1R (insulin-like growth factor 1 receptor) gene region at 15q25 is the most frequent anomaly found in CDH. The type 1 IGF receptor at 15q26 is required for normal embryonic and postnatal growth. Deletions, but also gain of an approximately 5 Mb region including the IGF1R gene, have been found to have a profound effect on prenatal and early postnatal growth.

The IGF1R (15q26) specific probe is optimized to detect copy numbers of the IGF1R gene region at region 15q26. The 15q11 (SNRPN / UBE3A) specific region probe is included to facilitate chromosome identification.

Cat.# KBI-40116 IGF1R (15q26) / 15q11





IGF1R (15q26) / 15q11 probe hybridized to patient material showing a deletion of the IGF1R gene region at 15q26 (1R2G).

Literature:

Faivre et al, 2002, Eur J Hum Genet. 10 ; 699-706.
Okubo et al, 2003, J Clin Endocrinol. Metab 88 ; 5981-5988.

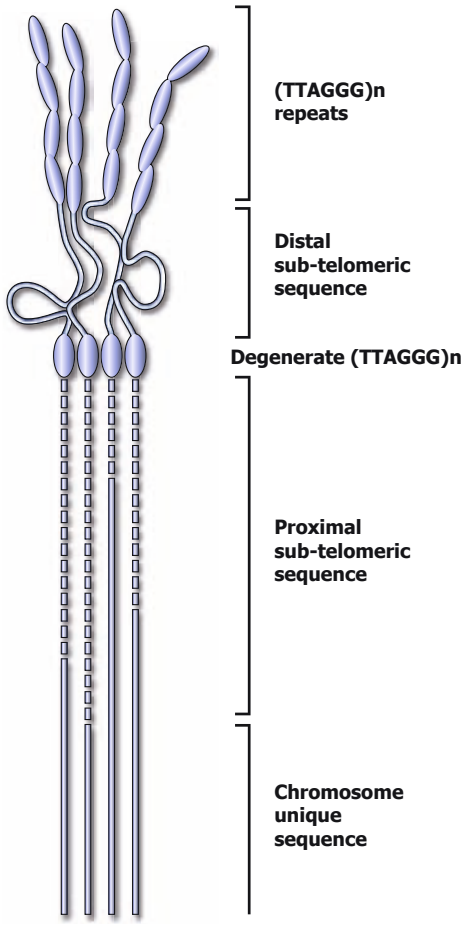
Ordering information	*Gene Region*	*Tests*	*Cat#*
MD IGF1R (15q26) / 15q11	IGF1R	10	KBI-40116

SUB-TELOMERE DNA PROBES

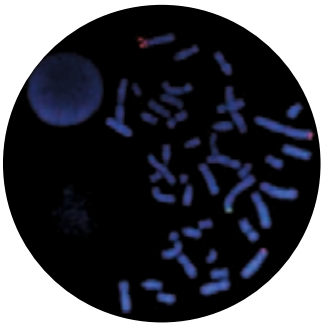
Telomeres are specialized DNA-protein structures containing long stretches of (TTAGGG)n repeats at the end of all chromosomes. They protect chromosomes from degradation and end-to-end fusion with other chromosomes. The region adjacent to sequences containing telomeric repeats is called the sub-telomer which has been found to be relative gene-rich. Cytogenetic analysis of sub-telomeric regions is difficult due to low resolution using conventional banding techniques. Cryptic deletions and rearrangements have been associated with unexplained mental retardation and congenital abnormalities. FISH probes specific for the sub-telomeric regions of the terminal chromosome regions are essential to detect such subtle rearrangements.

REPEAT-FREE™ POSEIDON™ Sub-Telomeric (ST) DNA Probes are supplied in a 5 test format together with hybridization buffer, direct labeled in either red (Platinum*Bright*™550), green (Platinum*Bright*495) or blue (Platinum*Bright*415). The ST probes are provided in a 5x concentrated format to allow, mixing of up to 5 ST probes in a single hybridization assay.

ST - Sub-Telomeric probes

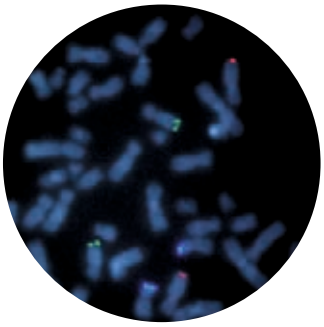


Dual-Color



Sub-Telomere probes 6pter and 2pter showing trisomy of tel 6p and monosomy of tel 2p.
Image kindly provided by Institute Pasteur, Paris.

Triple-Color



Combination of Sub-Telomere probes 6qter (red), 8qter (green) and 9pter (blue).

Product and ordering information

Location	*Marker*	*Probe Size (kb)*	*Distance from telomere (kb)*	*Color*	*Tests*	*Cat.# **
Sub-Telomere 1pter	D1S2217	170	800	red, green or blue	5	KBI-40201
Sub-Telomere 1qter	D1S555	170	350	red, green or blue	5	KBI-40202
Sub-Telomere 2pter	D2S2147	210	300	red, green or blue	5	KBI-40203
Sub-Telomere 2qter	D2S2142	185	800	red, green or blue	5	KBI-40204
Sub-Telomere 3pter	D3S4558	175	450	red, green or blue	5	KBI-40205
Sub-Telomere 3qter	D3S4168	170	900	red, green or blue	5	KBI-40206
Sub-Telomere 4pter	D4S3360	180	100	red, green or blue	5	KBI-40207
Sub-Telomere 4qter	D4S2283	190	700	red, green or blue	5	KBI-40208
Sub-Telomere 5pter	D5S2488	175	180	red, green or blue	5	KBI-40209
Sub-Telomere 5qter	D5S2006	270	600	red, green or blue	5	KBI-40210
Sub-Telomere 6pter	RH40931	110	350	red, green or blue	5	KBI-40211
Sub-Telomere 6qter	D6S2523	165	250	red, green or blue	5	KBI-40212
Sub-Telomere 7pter	D7S2644	220	850	red, green or blue	5	KBI-40213
Sub-Telomere 7qter	D7S427	180	200	red, green or blue	5	KBI-40214
Sub-Telomere 8pter	RH65733	180	550	red, green or blue	5	KBI-40215
Sub-Telomere 8qter	D8S595	210	200	red, green or blue	5	KBI-40216
Sub-Telomere 9pter	D9S917	190	450	red, green or blue	5	KBI-40217
Sub-Telomere 9qter	D9S1838	185	500	red, green or blue	5	KBI-40218
Sub-Telomere 10pter	D10S2488	180	350	red, green or blue	5	KBI-40219
Sub-Telomere 10qter	D10S2290	230	350	red, green or blue	5	KBI-40220
Sub-Telomere 11pter	D11S1363	155	1050	red, green or blue	5	KBI-40221
Sub-Telomere 11qter	D11S4437	170	300	red, green or blue	5	KBI-40222
Sub-Telomere 12pter	D12S158	185	150	red, green or blue	5	KBI-40223
Sub-Telomere 12qter	D12S399	190	180	red, green or blue	5	KBI-40224
Sub-Telomere 13qter	D13S1160	190	90	red, green or blue	5	KBI-40225
Sub-Telomere 14qter	D14S1419	170	250	red, green or blue	5	KBI-40226
Sub-Telomere 15qter	RH54179	150	250	red, green or blue	5	KBI-40227
Sub-Telomere 16pter	D16S521	150	40	red, green or blue	5	KBI-40228
Sub-Telomere 16qter	RH25942	180	240	red, green or blue	5	KBI-40229
Sub-Telomere 17pter	D17S643	110	80	red, green or blue	5	KBI-40230
Sub-Telomere 17qter	D17S724	70	500	red, green or blue	5	KBI-40231
Sub-Telomere 18pter	D18S1244	180	200	red, green or blue	5	KBI-40232
Sub-Telomere 18qter	D18S1390	220	160	red, green or blue	5	KBI-40233
Sub-Telomere 19pter	D19S814	220	550	red, green or blue	5	KBI-40234
Sub-Telomere 19qter	D19S989	160	300	red, green or blue	5	KBI-40235
Sub-Telomere 20pter	D20S1156	240	180	red, green or blue	5	KBI-40236
Sub-Telomere 20qter	RH44234	170	350	red, green or blue	5	KBI-40237
Sub-Telomere 21qter	D21S1446	190	80	red, green or blue	5	KBI-40238
Sub-Telomere 22qter	D22S1056	200	850	red, green or blue	5	KBI-40239
Sub-Telomere XYpter	DXYS130	180	400	red, green or blue	5	KBI-40240
Sub-Telomere XYqter	DXYS224	160	70	red, green or blue	5	KBI-40241

* Add -G for Green, -R for Red, -B for Blue (available on request)

SATELLITE ENUMERATION DNA PROBES

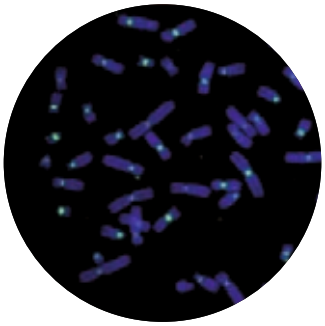
The primary constriction, called the centromer, is a common feature of chromosomes necessary for cell division. Presence of repetitive sequences in the centromeric regions have been proven to be essential. In humans, and many other species, specific repetitive sequences, called 'Satellites' are characteristic for the centromer in general. Most chromosomes also have repetitive sequences which are specific for individual chromosomes and can be used for precise identification and enumeration of human chromosomes in metaphase and interphase cells. The REPEAT-FREE™ POSEIDON™ Satellite Enumeration DNA probes allow rapid and specific chromosome analysis, marker chromosome identification and the detection of aneuploidy. Essentially, these probes can be used in all aspects of routine work in genetics and oncology/pathology. Due to the sharp and bright signals produced, the Satellite probes can easily be used on various sample types, such as cultured cells, touch preparations buccal smears, cytospins, frozen and paraffin-embedded tissue sections, sputum samples, sperm samples, and bladder washes.

POSEIDON Satellite Enumeration (SE) DNA Probes are supplied in a 10 test format together with hybridization buffer, direct labeled in either red (Platinum*Bright*™550), green (Platinum*Bright*495) or blue (Platinum*Bright*415). The SE probes are provided in a 5x concentrated format to allow, mixing of up to 5 SE probes in a single hybridization assay. The SE combination kits are supplied in a Ready-to-Use dual color format.

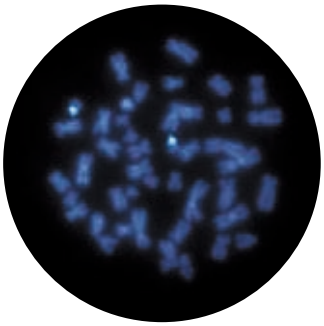
All Human Centromere (AHC) probe

This probe specifically hybridizes to the centromeric region of all human chromosomes, and is labeled with high fluorescence intensity in red or green color. POSEIDON™ AHC probe is ideal for studying numerical chromosome aberrations, studying aneuploidy, polyploidy, dicentrics, tricentrics, and other complex aberrations. It can also be used for general numerical chromosome analysis. POSEIDON AHC probe is for RUO and is not meant to be used for medical purposes or as a diagnostic tool.

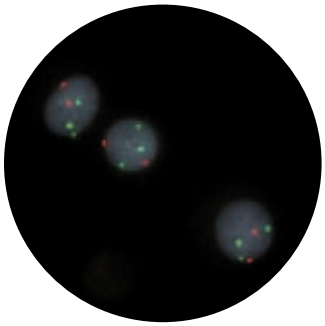
Cat.# KBI-20000 All Human Centromere (AHC) probe



Cat.# KBI-20000



Cat# KBI-20018-B



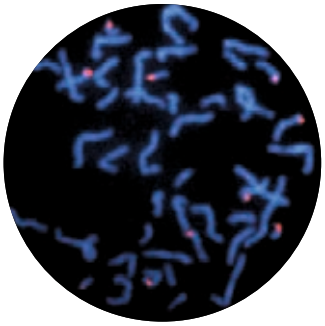
Cat# KBI-20031
SE7/SE8 showing trisomy 8.
Material kindly provided by Dr. Balogh, Budapest.

Note: Satellite sequences share some degree of homology between the sequences from chromosome to chromosome. Therefore the recommended stringency conditions in hybridization and posthybridization washes must be followed to provide optimal results. Chromosomes 1/5/19, 13/21, and 14/22 share the same repetitive sequences and cannot be differentiated by chromosome specific repeats.

Acro-P-Arms NOR

The NOR (Nucleolar Organizer Region) is located on every p-arm of the human acrocentric chromosomes. Enlargement of the acrocentric p-arms can be caused by an unusual variant or a translocation event. NOR stain of the p-arms is useful to detect such a p-arm variant. In the classification of small supernumerary marker chromosomes (SMCs) the Acro-P-Arms NOR probe can detect the origin of DNA, in which about 80% will turn out to be derived from the acrocentric chromosomes.

The Acro-P-Arms NOR probe is optimized to detect the short (p) arm of all acrocentric human chromosomes. The probe is intended to be used on metaphase/interphase spreads.



Cat# KBI-20033-R
Image kindly provided by Dr. Reboul, Nimes.

Literature:
Starke H et al., 2003, Hum Genet, 114; 51-67.
Starke H et al., 2005, J Histochem Cytochem, 53, 359-360.

Product and ordering information

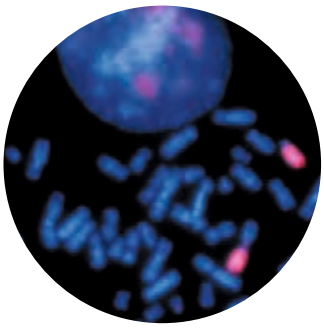
Description	*Chromosome*	*Color*	*DNA Class*	*Tests*	*Cat.# **
SE 1 (1qh)	1, 1qh	red, green or blue	Satellite III	10	KBI-20001
SE 2 (D2Z)	2	red, green or blue	α-satellite	10	KBI-20002
SE 3 (D3Z1)	3	red, green or blue	α-satellite	10	KBI-20003
SE 4 (D4Z1)	4	red, green or blue	α-satellite	10	KBI-20004
SE 6 (D6Z1)	6	red, green or blue	α-satellite	10	KBI-20006
SE 7 (D7Z1)	7	red, green or blue	α-satellite	10	KBI-20007
SE 8 (D8Z1)	8	red, green or blue	α-satellite	10	KBI-20008
SE 9 (classical)	9	red, green or blue	α-satellite	10	KBI-20009
SE 10 (D10Z1)	10	red, green or blue	α-satellite	10	KBI-20010
SE 11 (D11Z1)	11	red, green or blue	α-satellite	10	KBI-20011
SE 12 (D12Z3)	12	red, green or blue	α-satellite	10	KBI-20012
SE 15 (D15Z)	15	red, green or blue	α-satellite	10	KBI-20015
SE 16 (D16Z2)	16	red, green or blue	α-satellite	10	KBI-20016
SE 17 (D17Z1)	17	red, green or blue	α-satellite	10	KBI-20017
SE 18 (D18Z1)	18	red, green or blue	α-satellite	10	KBI-20018
SE 20 (D20Z1)	20	red, green or blue	α-satellite	10	KBI-20020
SE X (DXZ1)	X	red, green or blue	α-satellite	10	KBI-20023
SE Y (DYZ3)	Y, centromeric	red, green or blue	α-satellite	10	KBI-20024
SE Y classical (DYZ1)	Y, Yqh	red, green or blue	Satellite III	10	KBI-20025
SE 1/5/19 (D1Z7) (D5Z2) (D19Z3)	1, 5, 19	red, green or blue	α-satellite	10	KBI-20026
SE 13/21 (D13Z1) (D21Z1)	13 and 21	red, green or blue	α-satellite	10	KBI-20027
SE 14/22 (D14Z1) (D22Z1)	14 and 22	red, green or blue	α-satellite	10	KBI-20028
SE combinations					
SE X (DXZ1) / SE Y (DYZ3) RtU	X and Y	green/red	α-satellite	10	KBI-20030
SE 7 (D7Z1) / SE 8 (D8Z1) RtU	7 and 8	red/green	α-satellite	10	KBI-20031
AHC probe	All Human Centromere	red or green		10	KBI-20000
Acro-P-Arms NOR	13,14,15,21,22	red, green or blue		10	KBI-20033

* Add -G for Green, -R for Red, -B for Blue (available on request)

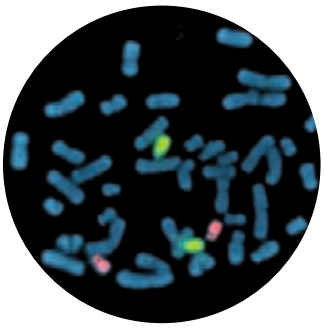
WHOLE CHROMOSOME DNA PROBES

The Whole Chromosome probes are used for identifying whole human chromosomes, analysis of translocation events, chromosome rearrangement studies and determining the origin of marker chromosomes. Mutagenesis analysis, radiation and sensitivity testing, and identification of human chromosomes on hybrid cells are investigated using these probes. The REPEAT-FREE™ POSEIDON™ Whole Chromosome DNA probes hybridize to unique sequences spanning the entire length of the target chromosome. These probes are derived from flow-sorted or microdissected chromosomes and provide accurate coverage with excellent signal specificity and high fluorescent intensity. Some minor cross-hybridization may occur at the short arm of acrocentric chromosomes (13, 14, 15, 21 and 22) and in the pseudo-autosomal regions of chromosome X and Y.

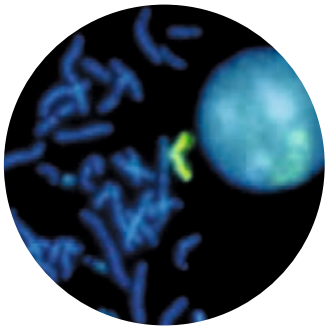
REPEAT-FREE POSEIDON Whole Chromosome (WC) DNA Probes are supplied in a 5 test format together with hybridization buffer, direct labeled in either red (Platinum*Bright*™550), green (Platinum*Bright*495) or blue (Platinum*Bright*415). The WC probes are provided in a 5x concentrated format to allow, mixing of up to 5 WC probes in a single hybridization assay.



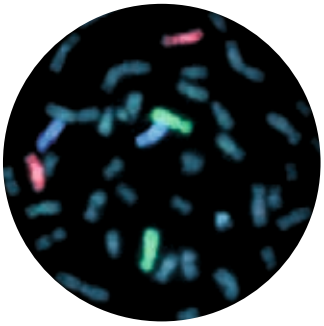
KBI-30013-R



WC Dual-Color



KBI-30023-G



WC Triple-Color

Note: Due to decondensation of chromosomal DNA signals on interphase, cells can be very diffuse. We therefore recommend not to use WC probes for interphase FISH.

Product and ordering information

Description	*Chromosome*	*Color*	*Tests*	*Cat.# **
Whole Chromosome 1	Chromosome 1 Paint	Red, green or blue	5	KBI-30001
Whole Chromosome 2	Chromosome 2 Paint	Red, green or blue	5	KBI-30002
Whole Chromosome 3	Chromosome 3 Paint	Red, green or blue	5	KBI-30003
Whole Chromosome 4	Chromosome 4 Paint	Red, green or blue	5	KBI-30004
Whole Chromosome 5	Chromosome 5 Paint	Red, green or blue	5	KBI-30005
Whole Chromosome 6	Chromosome 6 Paint	Red, green or blue	5	KBI-30006
Whole Chromosome 7	Chromosome 7 Paint	Red, green or blue	5	KBI-30007
Whole Chromosome 8	Chromosome 8 Paint	Red, green or blue	5	KBI-30008
Whole Chromosome 9	Chromosome 9 Paint	Red, green or blue	5	KBI-30009
Whole Chromosome 10	Chromosome 10 Paint	Red, green or blue	5	KBI-30010
Whole Chromosome 11	Chromosome 11 Paint	Red, green or blue	5	KBI-30011
Whole Chromosome 12	Chromosome 12 Paint	Red, green or blue	5	KBI-30012
Whole Chromosome 13	Chromosome 13 Paint	Red, green or blue	5	KBI-30013
Whole Chromosome 14	Chromosome 14 Paint	Red, green or blue	5	KBI-30014
Whole Chromosome 15	Chromosome 15 Paint	Red, green or blue	5	KBI-30015
Whole Chromosome 16	Chromosome 16 Paint	Red, green or blue	5	KBI-30016
Whole Chromosome 17	Chromosome 17 Paint	Red, green or blue	5	KBI-30017
Whole Chromosome 18	Chromosome 18 Paint	Red, green or blue	5	KBI-30018
Whole Chromosome 19	Chromosome 19 Paint	Red, green or blue	5	KBI-30019
Whole Chromosome 20	Chromosome 20 Paint	Red, green or blue	5	KBI-30020
Whole Chromosome 21	Chromosome 21 Paint	Red, green or blue	5	KBI-30021
Whole Chromosome 22	Chromosome 22 Paint	Red, green or blue	5	KBI-30022
Whole Chromosome X	Chromosome X Paint	Red, green or blue	5	KBI-30023
Whole Chromosome Y	Chromosome Y Paint	Red, green or blue	5	KBI-30024

* Add -G for Green, -R for Red, -B for Blue (available on request)

ARM SPECIFIC / BAND SPECIFIC DNA PROBES

Arm Specific Probes

In addition to our Whole Chromosome probes, we also provide the entire series of Arm Specific Probes (ASP). These probes hybridize to unique sequences comprising either p- or q-arms of all human chromosomes (except the p-arm of the acrocentric chromosomes), and they span the entire length of the respective chromosome arm. They are derived from flow-sorted or microdissected chromosomes, to be highly specific for each chromosome.

ASP applications permit the detection of chromosomal aberrations at the resolution of chromosome arms. This allows the analysis of chromosome partners involved in translocations, the identification of the chromosome of origin of marker chromosomes, analyses of complex chromosomal rearrangements in neoplastic cells and studying the inborn supernumerary marker chromosome as well as confirmation of results obtained from M-FISH and SKY testing. ASP may be of particular interest to those studying mutagenesis of human chromosomes, for instance as a result of exposure to genotoxic agents.

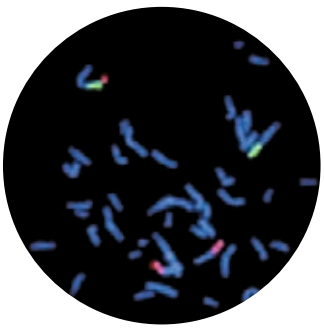
ASP are developed for Research Use Only (RUO) and are not meant to be used for medical purposes or as a diagnostics tool. Our Arm Specific Probes are supplied in a ready-to-use format, and are available in two colors of choice: green and red.

"Please note that only the Q arm is available for acrocentric chromosomes 13, 14, 15, 21 and 22. Heterochromatic areas (e.g. 1qh and 9qh) will not or only partially be covered by this type of probe. Due to the possibility of diffuse signals these ARM Specific Probes are not recommended for Interphase cell analysis."

Band Specific Probes

Rearrangements affecting regions smaller than an average G-band can be visualized using band-specific FISH probes. These particular probes enhance the resolution typically obtained with whole chromosome probes when identifying chromosomal abnormalities.

Band-Specific probes are capable of detecting small chromosomal segments, such as those involved in subtle translocations with breakpoints localized in distinct bands. They are amplified from microdissected chromosome material and fluorescently labeled to allow detection of these subchromosomal regions. For an updated list of Band-Specific probes please visit our website www.kreatech.com



Arm Specific Probes 2p and 6p showing a translocation of chromosome 2p on chromosome 6p.
Image kindly provided by Dr. Chantal Hamon, Paris.

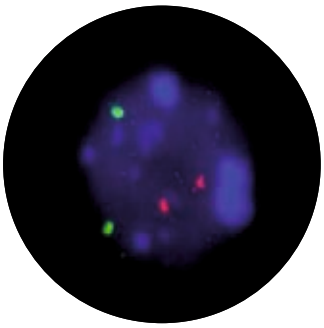
Product and ordering information

Description	*Color*	*Tests*	*Cat#*
Arm Specific Probe 1p	green or red	5	KBI-30100
Arm Specific Probe 1q	green or red	5	KBI-30101
Arm Specific Probe 2p	green or red	5	KBI-30102
Arm Specific Probe 2q	green or red	5	KBI-30103
Arm Specific Probe 3p	green or red	5	KBI-30104
Arm Specific Probe 3q	green or red	5	KBI-30105
Arm Specific Probe 4p	green or red	5	KBI-30106
Arm Specific Probe 4q	green or red	5	KBI-30107
Arm Specific Probe 5p	green or red	5	KBI-30108
Arm Specific Probe 5q	green or red	5	KBI-30109
Arm Specific Probe 6p	green or red	5	KBI-30110
Arm Specific Probe 6q	green or red	5	KBI-30111
Arm Specific Probe 7p	green or red	5	KBI-30112
Arm Specific Probe 7q	green or red	5	KBI-30113
Arm Specific Probe 8p	green or red	5	KBI-30114
Arm Specific Probe 8q	green or red	5	KBI-30115
Arm Specific Probe 9p	green or red	5	KBI-30116
Arm Specific Probe 9q	green or red	5	KBI-30117
Arm Specific Probe 10p	green or red	5	KBI-30118
Arm Specific Probe 10q	green or red	5	KBI-30119
Arm Specific Probe 11p	green or red	5	KBI-30120
Arm Specific Probe 11q	green or red	5	KBI-30121
Arm Specific Probe 12p	green or red	5	KBI-30122
Arm Specific Probe 12q	green or red	5	KBI-30123
Arm Specific Probe 13q	green or red	5	KBI-30124
Arm Specific Probe 14q	green or red	5	KBI-30125
Arm Specific Probe 15q	green or red	5	KBI-30126
Arm Specific Probe 16p	green or red	5	KBI-30127
Arm Specific Probe 16q	green or red	5	KBI-30128
Arm Specific Probe 17p	green or red	5	KBI-30129
Arm Specific Probe 17q	green or red	5	KBI-30130
Arm Specific Probe 18p	green or red	5	KBI-30131
Arm Specific Probe 18q	green or red	5	KBI-30132
Arm Specific Probe 19p	green or red	5	KBI-30133
Arm Specific Probe 19q	green or red	5	KBI-30134
Arm Specific Probe 20p	green or red	5	KBI-30135
Arm Specific Probe 20q	green or red	5	KBI-30136
Arm Specific Probe 21q	green or red	5	KBI-30137
Arm Specific Probe 22q	green or red	5	KBI-30138
Arm Specific Probe Xp	green or red	5	KBI-30139
Arm Specific Probe Xq	green or red	5	KBI-30140
Arm Specific Probe Yq	green or red	5	KBI-30141
Band Specific Probes - inquire	green or red	20	KBI-302xx

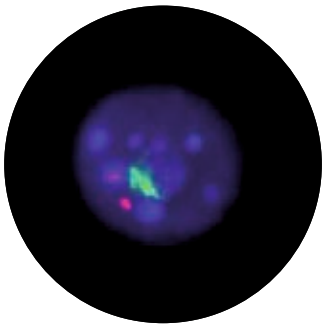
*Add -G for Green, -R for Red

MOUSE DNA PROBES

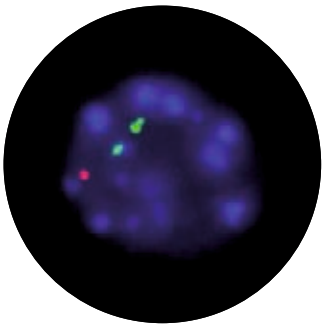
New applications for mouse molecular cytogenetics are becoming apparent. Such applications include the definition of transgene integration sites in epigenetics studies, the characterization of the mouse genome as a result of increasingly sophisticated techniques for its engineering and the screening for cytogenetic abnormalities in cell lines, such as embryonic stem cells. FISH mapping in mouse is complicated by the relative difficulty of mouse chromosome identification (karyotyping) by laboratories that are not accustomed to mouse chromosome banding techniques. Fluorescent karyotyping can be made easier by the use of counterstains or multiple reference probes but each approach needs specialized equipment and experience.



Cat.# KBI-30501

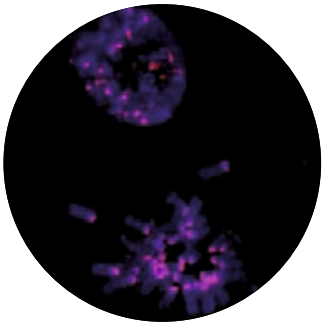


Cat.# KBI-30502



Cat.# KBI-30503

Kreatech has developed a couple of mouse region-specific probes prepared from defined BAC clones which are labeled with Platinum*Bright* dyes. These mouse probes are commonly used when developing model systems for studies in the field of genetics, mutagenesis, developmental cancer biology and also as human surrogates for studying the effects of genotoxic agents.



Cat.# KBI-30500
Hybridization of the All Mouse Centromere probe on mouse metaphase chromosomes.

Product and ordering information

Description	*Color*	*Tests*	*Cat#*
All Mouse Centromere (AMC)	red or green	10	KBI-30500
TK (11qE1) / AurKa (2qH3)	red/green	10	KBI-30501
TK (11qE1) / WC Y	red/green	10	KBI-30502
RAB9B (XqF1) / DSCR (16qC4)	red/green	10	KBI-30503
RAB9B (XqF1) / WC Y	red/green	10	KBI-30505

Further detailed information and the availability of these probes with other labels or other combinations are available on request.

Literature:
Sabhnani et al, 2011, Repr. BioMed. Onl, 22: 621-631.
Torchia et al, 2012, J of Inv. Derm, 133: 78–86.

CELL CULTURE MEDIA / ACCESSORIES

KREA*VITAL* CYTOGENETIC MEDIA

Our product line KREA*vital* and related products have been carefully selected to optimally address cytogenetic applications. They have been further optimized for best performance and undergo strict quality procedures ensuring consistent performance and superior results.

KREA*vital* Prenatal Medium (Complete)

The *in vitro* cultivation of amniotic fluid cells and chorionic villi is an essential part of every diagnostic cytogenetics laboratory, since the preparation of metaphase chromosome spreads is dependent upon obtaining cells in division. Amniocentesis and chorionic villi sampling are the major invasive diagnostic procedures used for the detection of fetal chromosomal abnormalities. KREA*vital* Prenatal Medium is specifically optimized for the primary culture of human amniotic fluid cells and chorionic villi samples used in prenatal diagnostic testing. The medium is contains serum, glutamine and antibiotics, and greatly reduces karyotyping time compared to conventional media.

In addition to the complete ready-to-use medium, we also provide KREA*vital* Prenatal as basal medium and supplement as separate components.

KREA*vital* Prenatal Medium PLUS (Complete)

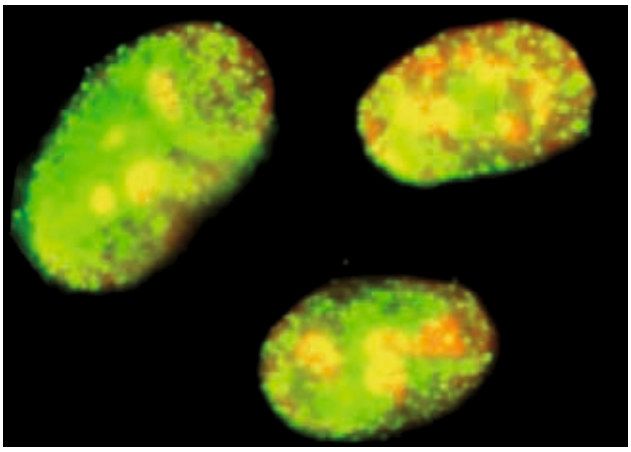
Growing cells from amniotic fluids yield a mixture of epithelial cells, fibroblasts and amniocytes. KREA*vital* Prenatal Medium PLUS is an optimized formulation specifically enriching for fibroblasts and amniocytes, which are the cells best suited for genetic analysis. This circumstance ensures optimal chromosome morphology and metaphase structure for microscopic observation, while reducing the relatively high background generated from having too much epithelial cells.

KREA*vital* Prenatal Medium PLUS provides

- Less epithelial cells
- Clearer chromosome morphology for optimal banding analysis
- Enhanced buffering capacity in closed systems
- Prolonged stability when stored at 4°C

KREA*vital* Lymphocyte Karyotyping Medium

KREA*vital* Lymphocyte Karyotyping Medium is intended for use in short-term cultivation of peripheral blood lymphocytes for chromosome evaluation. It is based on RPMI-1640 basal medium supplemented with L-Glutamine, fetal bovine serum and antibiotics. We provide this medium with and without the addition of phytohaemagglutinin (PHA), respectively.



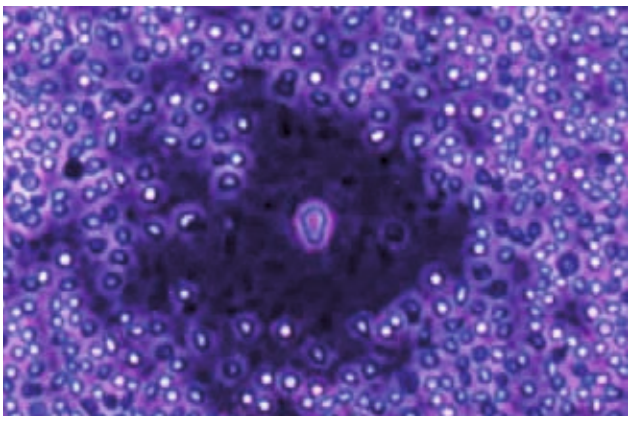
Human Amniocytes

KREA*vital* Bone Marrow Karyotyping Medium

An increasing number of cytogenetic analyses are carried out using bone marrow aspirates for studying chromosomal abnormalities in hematology. KREA*vital* Bone Marrow Karyotyping Medium is intended for use in short-term cultivation of primary bone marrow cells for chromosome evaluation and has been optimized for providing a high mitotic index. It is based on RPMI-1640 basal medium supplemented with L-Glutamine, fetal bovine serum, and antibiotics. The medium does not contain any mitogens or conditioned medium.

KREA*vital* Myeloid Cell Medium

Fresh cells or cells grown in short-term cultures often yield an insufficient number of mitotic cells and repeated aspirations are required. KREA*vital* Myeloid Cell Medium was developed to stimulate the proliferation of human hematopoietic cells from bone marrow as well as peripheral blood. This medium is particularly effective for karyotyping of acute non-lymphocytic leukemias and various stages of chronic myelogenous leukemia as well as other hematological disorders such as myelodysplastic syndrome and polycythemia vera. KREA*vital* Myeloid Cell Medium is based on MEM-Alpha basal medium supplemented with L-Glutamine, fetal bovine serum, antibiotics and conditioned medium.



Lymphocytes

All KREA*vital* media include L-Glutamine and antibiotics. To secure rigorous quality assurance, each KREA*vital* batch is tested for cell growth in a leading clinical cytogenetics laboratory.

Colchicine

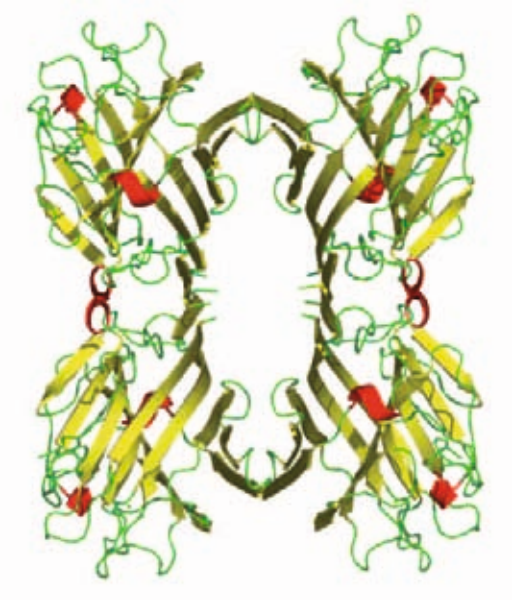
Colchicine is a secondary metabolite originally extracted from plants of the genus Colchicum. In cell biology it is traditionally used as a mitosis inhibitor to arrest cells in metaphase and allowing cell harvest and karyotyping to be performed.

Colcemid

Colcemid, also known as demecolcine, is related to colchicine, but less toxic, and therefore increasingly popular as an equivalent mitosis inhibitor in cytogenetics.

Phytohaemagglutinin

Phytohaemagglutinin (PHA) is a lectin found in plants, especially beans. It has a number of physiological effects and is used in medical research to trigger cell division in T-lymphocytes. In this function, PHA is the most commonly used agent to induce mitosis in nondividing cells, such as lymphocytes and mature cells. Our PHA is provided as the mucoprotein form (PHA-M). It is supplied sterile, in a lyophilized form for constituting 5 ml of solution.



Product and ordering information

Description	*contents*	*Cat#*
KREA*vital* Prenatal Medium (Basal)	90ml	KBI-90010
KREA*vital* Prenatal Medium (Basal)	450ml	KBI-92010
KREA*vital* Prenatal Medium (Supplement)	10ml	KBI-90011
KREA*vital* Prenatal Medium (Supplement)	50ml	KBI-92011
KREA*vital* Prenatal Medium (Complete)	100ml	KBI-90012
KREA*vital* Prenatal Medium (Complete)	500ml	KBI-92012
KREA*vital* Prenatal Medium PLUS (Complete)	100ml	KBI-90013
KREA*vital* Prenatal Medium PLUS (Complete)	500ml	KBI-92013
KREA*vital* Lymphocyte Karyotyping Medium (without PHA)	100ml	KBI-90020
KREA*vital* Lymphocyte Karyotyping Medium (without PHA)	500ml	KBI-92020
KREA*vital* Lymphocyte Karyotyping Medium (including PHA)	100ml	KBI-90021
KREA*vital* Lymphocyte Karyotyping Medium (including PHA)	500ml	KBI-92021
KREA*vital* Bone Marrow Karyotyping Medium	100ml	KBI-90030
KREA*vital* Bone Marrow Karyotyping Medium	500ml	KBI-92030
KREA*vital* Myeloid Cell Medium	100ml	KBI-90031
KREA*vital* Myeloid Cell Medium	500ml	KBI-92031
Accessories		
Colchicine Solution (10µg/ml, in PBS)	25ml	KBI-90050
Colcemid Solution (10µg/ml, in PBS)	10ml	KBI-90051
Potassium Chloride (0.075M)	100ml	KBI-90052
Phytohaemagglutinin M-Form	5ml	KBI-90053
Sodium Citrate Solution (0.8%)	500ml	KBI-90054
Trypsin EDTA 10X (EDTA 0.2%, Trypsin 0.5%, in saline solution)	20ml	KBI-90055
Trypsin EDTA 10X (EDTA 0.2%, Trypsin 0.5%, in saline solution)	100ml	KBI-92055

PRETREATMENT KITS / REAGENTS

The ready-to-use pretreatment kits are recommended to be used with POSEIDON™ FISH DNA probes to produce high quality results. The kits contain all necessary ready-to-use reagents used for slide pretreatment and washing steps for FISH. The reagents increase the permeabilization of the cell membranes to facilitate penetration of the POSEIDON FISH DNA probes. The pretreatment kits will allow to process up to 25 slides in batches of 5 slides per experiment.

Pretreatment Kits

FISH Reagent Kit (KBI-60005)

FISH Reagent Kit contains all necessary ready-to-use reagents to be used for basic pretreatment of freshly prepared cytological samples.

FISH Digestion Kit (KBI-60006)

FISH Digestion Kit consists of ready-to-use reagents designed to obtain optimal results with older/difficult cytological samples or samples with cytoplasmic background which have been fixed in alcohol based fixatives (e.g. Carnoy's). Reagents provided allow to perform mild digestion on difficult cytogenetic samples, such as uncultured amniocytes, direct blood smears, buccal scrapings, urine, touch preps and others.

Tissue Digestion Kit I (KBI-60007)

Tissue Digestion Kit I contains all necessary ready-to-use reagents to be used for pretreatment of conventional paraffin-embedded tissues.

Tissue Digestion Kit II (KBI-60004)

Tissue Digestion Kit II contains all necessary ready-to-use reagents to be used for pretreatment of heavily cross-linked paraffin-embedded tissue. The Tissue Digestion Kit II provides a more intense pretreatment for optimal performance.

The selection table can guide you which pretreatment kit is the most optimal for your sample type:

Sample	KBI-60005	KBI-60006	KBI-60007	KBI-60004
Freshly prepared cytological samples	+	(+)		
Older / difficult / cytological samples	(+)	+		
Standard tissue			+	(+)
Heavily cross-linked tissue			(+)	+

Reagents

FISH Hybridization Buffer

FISH Hybridization Buffer (FHB) is a ready-to-use hybridization solution used for ULS™ labeled FISH DNA probes. FHB contains formamide, SSC, and Dextran Sulfate. Qualified for use for standard cytological and all kind of direct samples (uncultured amniocytes, blood, bone marrow, buccal scrapin, urine etc.). FHB is provided with all POSEIDON Satellite Enumeration and Sub-Telomeric probes to obtain a ready-to-use format.

Paraffin Tissue Buffer

Paraffin Tissue Buffer (PTB) is a ready-to-use hybridization solution for ULS labeled FISH DNA probes. PTB contains formamide, SSC, and Dextran Sulfate. Qualified for use on Paraffin tissues.

Whole Chromosome Buffer

Whole Chromosome Buffer (WCB) is a ready- to- use hybridization solution for ULS labeled Whole Chromosome probes. WCB contains formamide, SSC, and Dextran Sulfate. Qualified for use on standard cytological samples. WCB is provided with all POSEIDON Whole Chromosome probes.

Rubber Cement, Fixogum

For use in the formation of an air tight seal around the perimeter of the glass coverslip during probe hybridization for FISH.

Product and ordering information

Description	*Contents*	*Cat#*
POSEIDON™ Tissue Digestion Kit II	5x5 slides	KBI-60004
POSEIDON FISH Reagent Kit	5x5 slides	KBI-60005
POSEIDON FISH Digestion Kit	5x5 slides	KBI-60006
POSEIDON Tissue Digestion Kit I	5x5 slides	KBI-60007
Rubber Cement, Fixogum	125 ml	LK-071A
DAPI Counterstain (0.1µg/ml)	1 ml	LK-095A
DAPI Counterstain (1µg/ml)	1 ml	LK-096A
Counterstain Diluent	1 ml	LK-097A
Pepsin Solution	2.5 ml	LK-101A
Wash Buffer I (0.4 x SSC/0.3% Igepal)	100 ml	LK-102A
Wash Buffer II (2 x SSC/0.1% Igepal)	100 ml	LK-103A
FISH Hybridization Buffer (FHB)	100 µl	KBI-FHB
Paraffin Tissue Buffer (PTB)	100 µl	KBI-PTB
Whole Chromosome Buffer (WCB)	50 µl	KBI-WCB

EQUIPMENT

ThermoBrite™

This programmable system automates the denaturation and hybridization steps in slide-based in situ hybridization procedures, and provides walk-away convenience for clinical and research personnel. The ThermoBrite accepts a wide range of sample types, is easy to use, and reduces hands-on time by more than 50% while ensuring overall precision and accuracy in all FISH assays.

Thermobrite
Slide Denaturation
Hybridization System

The ThermoBrite accommodates up to 12 slides and maintains uniform temperature across all slide positions. The lid seals tightly when closed providing optimal chamber humidity. The numeric keypad allows for easy programming with 40 user programmable settings and 3 modes of operation; denaturation/hybridization, hybridization, and fixed temperature.

ThermoBrite and CytoFuge 2 are trademarks of StatSpin, a division of IRIS Sample Processing.

CytoFuge® 2

The Cytofuge 2 is a low cost personal cytocentrifuge. It has simply understandable controls and new snap-seal Filter Concentrators that make operation easy. Samples are processed quickly, silently, and conveniently on any bench or in a safety cabinet. Results are consistent: easy to scan monolayer cell presentations of excellent morphologic detail.

The CytoFuge 2
is ideal for a complete range of body fluids:
- Pleural fluids
- Sputum
- Urine
- Synovial fluids
- Fine needle aspirates
- Bronchial washings
- Cerebrospinal fluids

Specifications

Safety features:	Cover interlock system Leak-resistant rotor with transparent lid Low voltage drive system (24V) Designed to meet requirements of IEC-1010-2-020	
Rotor capacity:	One to four slides	
Speed:	600 RPM (20 x g) 700 RPM (27x g) 850 RPM (40 x g) 1000 RPM (55 x g)	1300 RPM (93 x g) 1600 RPM (140 x g) 2200 RPM (265 x g) 4400 RPM (1060 x g)
Dimensions:	15,2 cm x 16,8 cm x 21,8 cm	
Weight:	2,5 kg	

Product and ordering information

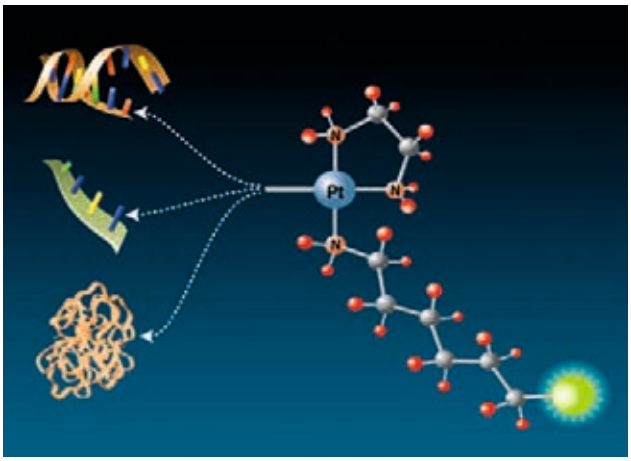
Description		*Cat#*
ThermoBrite (120V, 50-60Hz)		TS-01
ThermoBrite (240V, 50-60Hz)		TS-02
Humidity Control Cards	10	HC-10
Cytofuge2 (100 - 240V, 50 / 60 Hz)*		CF-02
Reusable Filter Concentrators	20	FFR1
Filter Concentrators (disposable)	192	FF01-B

*) not available in all countries. Please inquire

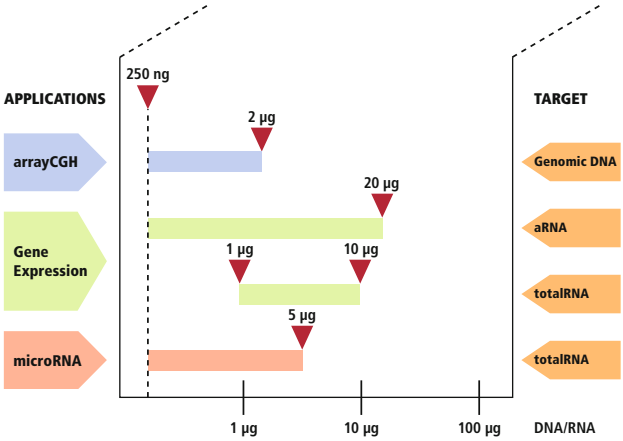
THE ULS LABELING TECHNOLOGY

The proprietary ULS™ (Universal Linkage System) technology provides the basis for KREATECH's broad range of labeling applications. ULS labeling is based on the stable coordinative binding properties of platinum to nucleic acids and proteins. The ULS molecule consists of a platinum complex, a detectable molecule and a leaving group which is displaced upon reaction with the target. This reaction results in a coordinative bond, firmly coupling the ULS to the target. ULS labels DNA and RNA by binding to the N7 position of guanine. In proteins, ULS binds to sulfur and nitrogen containing side chains of methionine, cysteine and histidine. ULS is coupled to a variety of fluorophores and haptens.

Principle of the ULS technology



Optimal template amount for using Kreatech's ULS labeling kits



Targets labeled with ULS

Nucleic Acids	Proteins
Guanine	Methionine, Cysteine, Histidine
ULS labels DNA and RNA by forming a coordinative bond on the N7 position of guanine	ULS labels proteins by forming a coordinative bond on the sulfur atoms of methionine, cysteine and the nitrogen atom of histidine

Unique features of the ULS Labeling Technology

- Time saving: Entire labeling procedure in only 30 minutes for DNA and 15 minutes for RNA
- Extremely easy to use
- Robust and reproducible – no enzymes involved
- Superior labeling technology for FFPE samples
- One technology for labeling DNA, RNA and proteins
- Compatible with all types of microarray platforms.

Table of Contents

ARRAYCGH

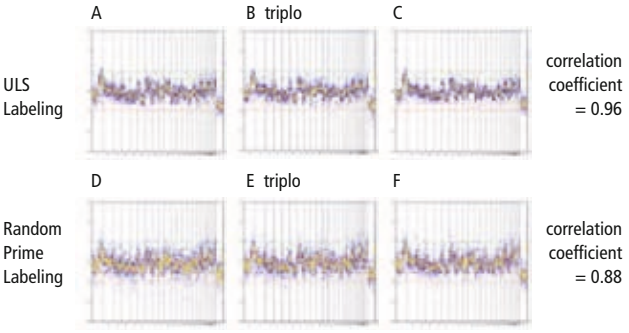
ULS™ arrayCGH Labeling Kit

The ULS arrayCGH Labeling Kit offers a novel procedure that allows direct (non-enzymatic) labeling of both intact genomic DNA as well as fragmented genomic DNA isolated from formalin-fixed paraffin-embedded (FFPE) samples. The ULS arrayCGH Labeling Kit yields highly reproducible fluorescent labeled DNA within minutes. The ULS technology has been validated on a wide range of oligo and BAC arrayCGH platforms. All ULS kits for arrayCGH analysis include the KREA*pure* purification technology and KREA*block* blocking reagents to ensure efficient purification of labeled DNA samples and low background levels during hybridization.

Unique features of ULS arrayCGH Labeling Kit

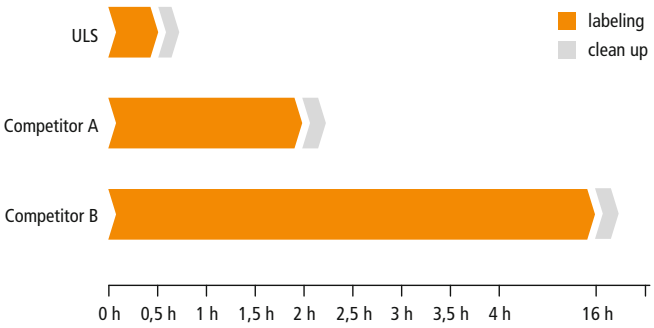
- 30-minute labeling procedure
- Labeling independent of fragment size - ideal for FFPE samples
- ULS labeling is not affected by cross links present in genomic DNA from FFPE samples
- No enzymatic bias
- KREA*pure* column purification ideally suited for fragmented DNA
- No bias when amplified DNA need to be labeled.

ULS Labeling vs Random Prime Labeling



Ratio plots of 3 independent array CGH hybridizations using genomic DNA from healthy liver which is the reference vs. genomic DNA isolated from a liver tumor FFPE sample. (A-C) ULS labeled samples. (D-F) Random Prime labeled samples.

Time of ULS labeling vs. enzymatic labeling procedure



Product and ordering information

Description	*Contents*	*Cat#*
arrayCGH Labeling		
ULS arrayCGH Labeling Kit (with Cy3 and Cy5)	for labeling 2 x 20 µg DNA	EA-005
ULS arrayCGH Labeling Kit (with Cy3)	for labeling 40 µg DNA	EA-005A
ULS arrayCGH Labeling Kit (with Cy5)	for labeling 40 µg DNA	EA-005B

DNA PRODUCTS

ArrayGrade KREA*cot* DNA

ArrayGrade KREA*cot* DNA is extracted from human placental DNA and subsequently fragmented, denatured, and re-annealed under conditions that enrich for repetitive DNA sequences (1,2). ArrayGrade KREA*cot* DNA can be used to suppress cross-hybridization to human repetitive DNA sequences. ArrayGrade KREA*cot* DNA has specifically been optimized to be used in array CGH applications. Amounts of ArrayGrade KREA*cot* DNA needed in a microarray experiment should be determined empirically, but will be in the order of 12.5-50 times excess to the amount of labeled genomic DNA. In addition, ArrayGrade KREA*cot* is suitable for blocking repetitive sequences during the target enrichment procedure for high throughput sequencing purposes. Please visit the Kreatech website (www.kreatech.com) for a detailed protocol for the analysis of genomic DNA using arrayCGH.

Unique features of ArrayGrade KREA*cot*

- Specifically optimized for use in arrayCGH applications
- Quality controlled with arrayCGH analysis.

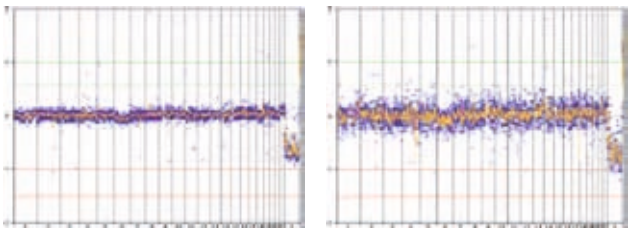
Megapool Reference DNA

This product is a homogeneous DNA pool from male or female human genomic DNA which has been isolated from 100 different anonymous healthy individuals. The genomic DNA is of high quality and the DNA from each of these 100 individuals contributes evenly to the DNA pool. This product is specifically developed as a reference for genomic microarray-based comparative genomic hybridization experiments (array CGH).

Unique features of the MegaPool Reference DNA

- The product will guarantee perfectly comparable profiles for male and female individuals as well as complete absence of pure homozygous deletions
- Sex-matched arrayCGH experiments will be possible and enable high-quality genotyping data for both chromosomes X and Y as well as unbiased CNV profiles between male and female test samples.

Comparison of performance of ArrayGrade KREA*cot* DNA and human C0t-1 DNA from competitor X.



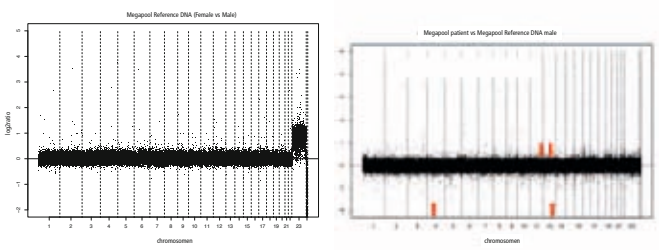
ArrayGrade KREA*cot*
^{2}log ratio for X chromosome = -0.65
Mean absolute deviation for chrom 1-22 = 0.05

Human C_0t-1 DNA competitor X
^{2}log ratio for X chromosome = -0.66
Mean absolute deviation for chrom 1-22 = 0.11

Shown are the chromosome plots obtained from an arrayCGH hybridization comparing healthy male Cy5-ULS labeled genomic DNA and healthy female Cy3-ULS labeled genomic DNA on BAC microarrays. Although the spread observed for the X-chromosome is comparable for both blockers, the use of ArrayGrade KREA*cot* minimizes the variation observed for chromosomes 1-22.

Megapool Reference DNA (Female vs Male)

Male patient vs. Male Megapool Reference DNA



Left: Female Megapool Reference DNA is hybridized against the Male Megapool Reference DNA on an Agilent's 4 x 180 k human aCGH array. The X and Y chromosomes can be clearly identified. The Derivative Log-Ratio Spread (DLRS) value is **0.084** which is considered as excellent.

Right: Male Megapool Reference DNA is hybridized against a male mental retardation patient on an Agilent's 4 x 180k human aCGH array. Variations are clearly visible at Chromosomes 5, 15 and 16. The Derivative Log-Ratio Spread (DLRS) value is **0.1189**. Data are kindly provided by Bauke Ylstra and colleagues VU University Medical Center, Amsterdam.

Product and ordering information

Description	*Contents*	*Cat#*
ArrayGrade KREA*cot* DNA	500 µg	EA-020
ArrayGrade KREA*cot* DNA	10 mg	EA-035
Megapool Reference DNA (male)	200 µg	EA-100M
Megapool Reference DNA (female)	200 µg	EA-100F

GENE EXPRESSION

Amplification and aRNA Labeling Kits

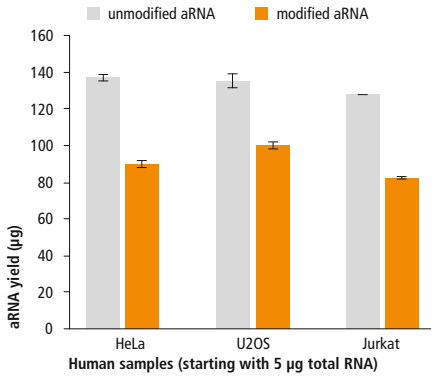
aRNA Labeling Kits

The Universal Linkage System (ULS™) allows direct labeling of unmodified, amplified RNA (aRNA). Specific aRNA labeling kits are both available for the use with commercial platforms from Agilent, Affymetrix® (Genechips®) and CombiMatrix, and for the use with self-spotted DNA arrays.

Unique features of aRNA Labeling Kits

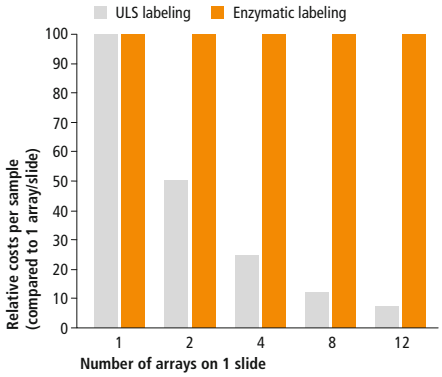
- Higher yields of unmodified aRNA compared to modified aRNA
- Storage of unmodified aRNA for subsequent use possible
- No waste of labeled material; label only the amount aRNA needed
- Reduced labeling cost per hybridization when using multiple arrays per slide.

Higher yields of unmodified aRNA as compared to modified aRNA



Unmodified antisense RNA (aRNA) vs. modified aRNA.

Lower cost if multiple arrays per slide are used



Costs for ULS labeling of unmodified aRNA vs. costs for enzymatic labeling generating modified aRNA.

Product and ordering information

Description	*Contents*	*Cat#*
aRNA Labeling		
ULS aRNA Labeling Kit (with Cy3 and Cy5)	for labeling 2 x 50 µg aRNA	EA-006
ULS aRNA Labeling Kit (with Biotin for Affymetrix Genechips)	for labeling 500 µg aRNA	EA-010
ULS aRNA Labeling Kit (with Biotin)	for labeling 250 µg aRNA	EA-018
ULS Fluorescent Labeling Kit for Agilent arrays (with Cy3 and Cy5)	for labeling 2 x 50 µg aRNA	EA-021
ULS Fluorescent Labeling Kit for Agilent arrays (with Cy5)	for labeling 50 µg aRNA	EA-022
ULS Fluorescent Labeling Kit for Agilent arrays (with Cy3)	for labeling 50 µg aRNA	EA-023
ULS Labeling Kit for CombiMatrix arrays (with Cy5)	for labeling 125 µg aRNA	EA-025
ULS Labeling Kit for CombiMatrix arrays (with Biotin)	for labeling 125 µg aRNA	EA-027

MICRORNA

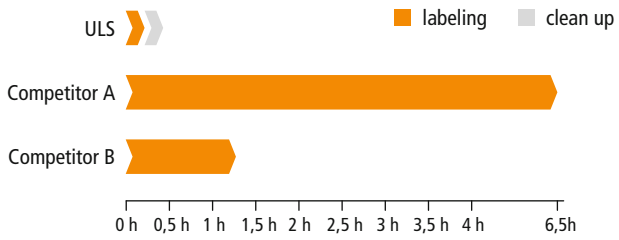
microRNA Labeling Kit

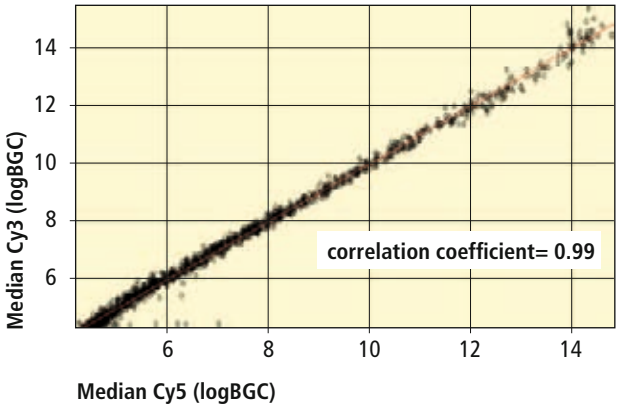
The new ULS microRNA Labeling Kit provides a very simple and fast method for miRNA detection on microarray platforms. The Universal Linkage System (ULS) labeling technology is used to directly label the naturally occurring miRNAs which are present in the total RNA mixture without the need to enrich for small RNA. ULS can be used to label total RNA from all kind of organisms.

Unique features of the ULS microRNA Labeling Kit

- 15-minute labeling step
- Easy two-step procedure to label total RNA
- Compatible with most existing miRNA platforms
- Not size discriminative.

Time of ULS labeling vs. competitive labeling technologies.





Product and ordering information

Description	*Contents*	*Cat#*
microRNA Labeling		
ULS microRNA Labeling Kit (with Cy3 and Cy5)	for labeling 2 x 25 µg RNA	EA-036
ULS microRNA Labeling Kit (with Cy3)	for labeling 50 µg RNA	EA-037
ULS microRNA Labeling Kit (with Cy5)	for labeling 50 µg RNA	EA-038

GENERAL NUCLEIC ACID LABELING

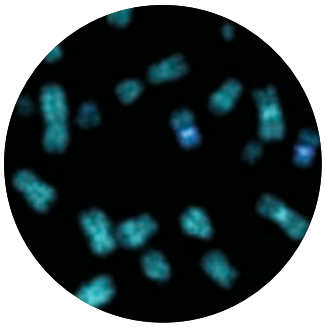
PLATINUM*Bright*™ Labeling Kits

The Platinum*Bright* Nucleic Acid Labeling Kits are based on KREATECH's patented Universal Linkage System (ULS). The ULS molecule is a proprietary platinum compound linked to a hapten or a fluorophore. The Platinum*Bright* kits offer ULS coupled to a variety of fluorophores or biotin providing a non-enzymatic, easy-to-use alternative to conventional techniques such as nick translation, random priming, end labeling, etc.

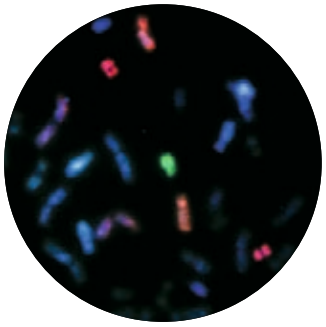
The labeled nucleic acid can be used for the downstream application of your choice. In addition to the Platinum*Bright* Nucleic Acid Labeling Kits, KREATECH also offers the FISH*Bright* kits which, in addition to reagents for labeling, include all reagents needed for FISH hybridization.

Unique features of the Platinum*Bright* Labeling Kits

- Only a two-step, very fast labeling procedure
- Easy to perform
- A variety of labels to choose from
- Not dependent on the performance of enzymes.



Centromere 11 labeled with Platinum*Bright* 415.



4-color FISH.

FISH*Bright*™ labeling kits

The FISH*Bright* labeling kits are based on KREATECH's Universal Linkage System (ULS™). The ULS molecule is a proprietary platinum compound linked to a hapten or a fluorophore. The FISH*Bright* kits offer ULS molecules coupled to a variety of fluorophores or haptens providing a non-enzymatic, easy-to-use alternative to conventional techniques such as nick translation, random priming, end labeling, etc.

The FISH*Bright* labeling kits are specially developed for FISH applications: labeled DNA probes can be used on all type of samples including metaphase spreads, direct interphase cell preparation (e.g. blood smears, bone marrow smears, urine samples, paraffin-embedded or frozen tissue sections).

KREATECH's REPEAT-FREE™ POSEIDON™ DNA probes are labeled with the same technology and all POSEIDON pretreatment kits can be used in combination with DNA probes which are labeled with the FISH*Bright* labeling kits.

Besides the ULS technology, the kits also contain Cell specific Hybridization Buffer (CHB), and Tissue Hybridization Buffer (THB). In addition, the KREA*boost* solution, which is developed to generate a high signal-to-noise ratio especially on paraffin-embedded tissue sections, is included in these kits.

The FISH*Bright* labeling kits will offer you all advantages of the ULS technology:

- Easy to use
- 30-minute labeling procedure
- Use of KREA*pure* columns: a unique purification column which guarantees a very high removal of non-reacted ULS (> 99%) and high sample recoveries (> 95%).

Content:

- Platinum*Bright* component (fluorochromes or haptens)
- 10 x labeling solution
- KREA*pure* purification columns
- Hybridization buffer for cytological preps (CHB)
- Hybridization buffer for paraffin preps (THB+KREA*boost*).

The FISH*Bright* kit contains sufficient solution to label up to 10 µg of BAC DNA, which generally allows for 100 or more FISH assays using 10 µl labeled probe in hybridization buffer (amount of FISH assays is dependent on the final concentration of labeled DNA. Usually 50 – 100 ng/µl of labeled BAC DNA is necessary per assay).

FISHgrade C_0t

FISHgrade C_0t DNA is extracted from human placental DNA treated under conditions that enrich for repetitive DNA sequences (1,2). These conditions have been optimized by Kreatech Diagnostics for the specific use in FISH experiments.

FISHgrade C_0t DNA suppresses cross-hybridization to human repetitive DNA. Amounts of FISHgrade C_0t DNA needed in a FISH experiment should be determined empirically, but will be in the order of 12.5 – 50 times excess to the amount of labeled genomic DNA.

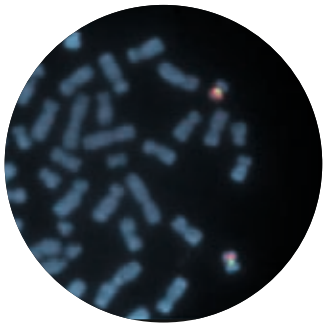
Unique features of FISHgrade C_0t

- High quality human C_0t-1 DNA optimized for use in FISH application
- Specific quality control with FISH analysis
- Works perfectly for probes labeled with FISH*Bright* ULS-Kits.

References

1. Weiner, A.M., et al. (1986) Ann. Rev. Biochem. 55, 631.
2. Britten, R.J., et al. (1974) Methods Enzymol. 29, 363.

Cat.# KB-COT FISHgrade Cot



FISH image on metaphase spread performed using a classical FISH probe labeled in red/green colors using a FISH*Bright*™ labeling kit. FISHgrade C0t DNA has been used to block all aspecific DNA sequences. The probe specifically recognizes deletions at 20q chromosome that have been related to myelodysplastic syndromes.

Product and ordering information

Description	*Color*	*Excitation/Emission*	*Contents*	*Cat#*
Platinum*Bright*™ Nucleic Acid Labeling Kit (495 Green)		495/517	for labeling 20 µg template	GLK-001
Platinum*Bright* Nucleic Acid Labeling Kit (547 Light Red)		547/565	for labeling 20 µg template	GLK-002
Platinum*Bright* Nucleic Acid Labeling Kit (647 Far Red)		647/665	for labeling 20 µg template	GLK-003
Platinum*Bright* Nucleic Acid Labeling Kit (550 Red)		550/580	for labeling 20 µg template	GLK-004
Platinum*Bright* Nucleic Acid Labeling Kit (415 Blue)		429/470	for labeling 20 µg template	GLK-006
Platinum*Bright* Nucleic Acid Labeling Kit (Biotin)			for labeling 20 µg template	GLK-007
FISH*Bright*™ Labeling Kit (415 Blue)		429/470	for labeling 10 µg DNA	FLK-001
FISH*Bright* Labeling Kit (495 Green)		495/517	for labeling 10 µg DNA	FLK-002
FISH*Bright* Labeling Kit (505 Green)		500/528	for labeling 10 µg DNA	FLK-003
FISH*Bright* Labeling Kit (550 Red)		550/580	for labeling 10 µg DNA	FLK-004
FISH*Bright* Labeling Kit (547 Light Red)		547/565	for labeling 10 µg DNA	FLK-005
FISH*Bright* Labeling Kit (647 Far Red)		647/665	for labeling 10 µg DNA	FLK-006
FISH*Bright* Labeling Kit (Biotin)			for labeling 10 µg DNA	FLK-007
FISH Grade CoT			500 µg	KB-COT

PROTEIN LABELING / **ANTIBODY** LABELING

Platinum*Link* Antibody Labeling Kits

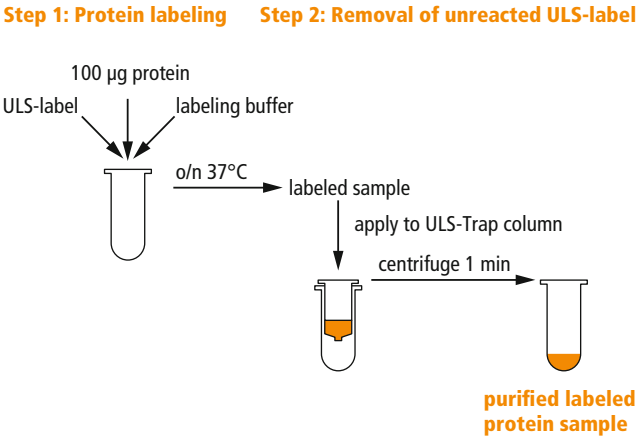
The Platinum*Link* Kits provide high coverage of the proteome through specific labeling of methionine, cysteine and histidine residues. Unlike lysine, which is targeted by N-hydroxysuccinimidyl (NHS) esters, the amino acids labeled with ULS are less likely to be involved in protein - protein interactions. Therefore, labeling of proteins and antibodies with ULS will reduce negative effects on interaction domains and epitope recognition.

The Platinum*Link* Antibody Labeling Kits have been optimized to label 100 µg of purified antibody (or recombinant protein) per reaction with fluorescent dyes or haptens.

Unique features of the Platinum*Link* Antibody Labeling Kits

- Easy and robust labeling of antibodies and recombinant proteins
- ULS-Trap removes unreacted label, no size exclusion
- Labeling of methionines, cysteines and histidines in antibodies and recombinant proteins
- Labeling reaction is independent of pH
- Compatible with commonly-used detergents including Tris-HCl.

Schematic overview of the Platinum*Link* labeling procedure.



Recovery comparison of different proteins.

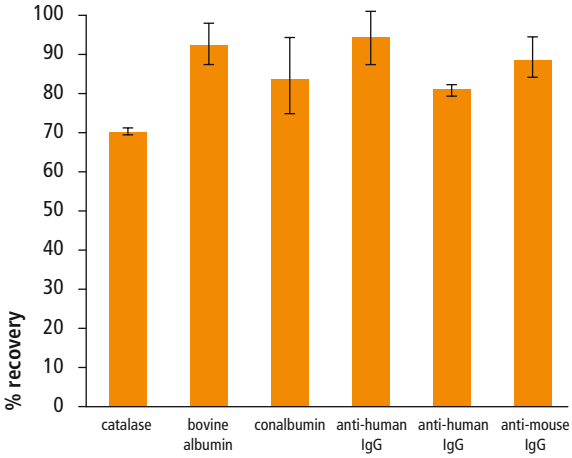


Fig.18 Protein recovery using ULS-Trap columns. 100 µg of protein was labeled and purified using Platinum*Link* protein labeling kits. Protein concentration was determined using Biorad's Rc Dc protein assay. Recovery is presented as percentage protein recovered as compared to unpurified sample.

Product and ordering information

Description	*Reactions*	*Cat#*
Platinum*Link* Protein Labeling Kit (BIO)	4 single labelings	PLK-007
Platinum*Link* Protein Labeling Kit (FLU)	4 single labelings	PLK-009
Platinum*Link* Protein Labeling Kit (RHO)	4 single labelings	PLK-010

SUPPORTING PRODUCTS

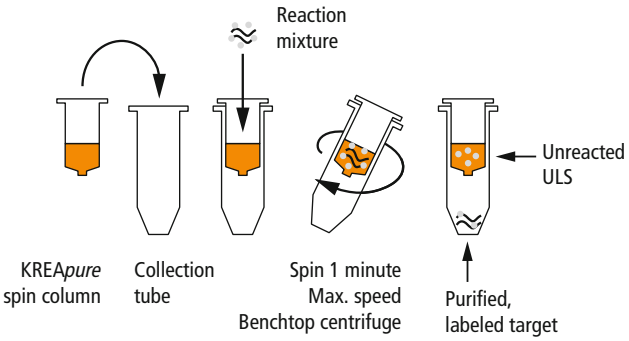
KREA*pure*™ purification columns and plates

KREA*pure* purification columns and plates are based on a proprietary purification matrix optimized for purifying ULS-labeled target nucleic acids. The procedure quantitatively removes non-attached label and provides optimal recovery of labeled nucleic acids.

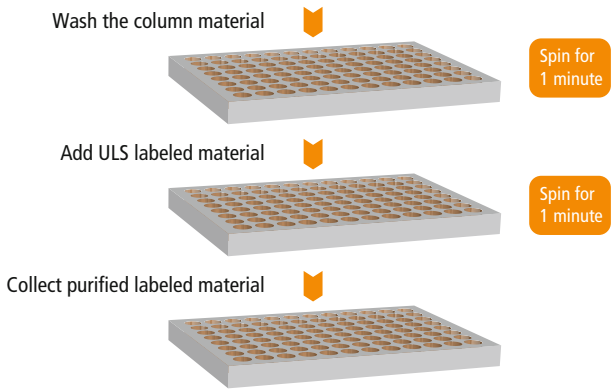
Unique features of the KREA*pure* purification

- Maximal removal of unreacted ULS-label
- > 95% recovery of labeled nucleic acid
- Efficient recovery of small fragments

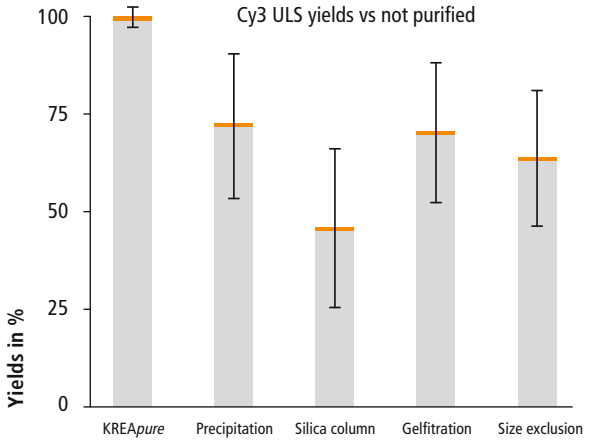
KREA*pure* spin column purification.



KREA*pure* 96-well procedure.



Yield comparison of different purification methods.



Cy3 – ULS-labeled DNA has been purified using five different purification systems. Experiments were performed in triplicate.

Product and ordering information

Description	*Reactions*	*Cat#*
KREA*pure* ™ columns	20 pcs	KP-020
KREA*pure* columns	50 pcs	KP-050
KREA*pure* 96*	1 plate	KP-096

** specific high-throughput labeling modules available upon request*

PRODUCT INDEX

CATALOGUE 2013-2014 - NEW PRODUCTS

ON = Oncology probes

	Description	Color	Tests	Cat#	Page
ONCOLOGY - HEMATOLOGY DNA PROBES					
CML	ON Mm-BCR/ABL t(9;22), DC, S-Fusion, ES	green/red	10	KBI-10013	II
AML	ON MECOM / RUNX1 t(3;21) Fusion	red/green	10	KBI-10310	II
	ON NUP98 (11p15) Break	red/green	10	KBI-10311	III
ALL	ON MLL/AFF1 t(4;11) Fusion	red/green	10	KBI-10404	III
MM	ON MAFB/IGH@ t(14;20) Fusion	red/green	10	KBI-10510	IV
ONCOLOGY – SOLID TUMOR DNA PROBES					
Lung Cancer	ON ROS1 (6q22) Break	green/red	10	KBI-10752	V
	ON RET (10q11) Break	green/red	10	KBI-10753	V
	ON FGFR1 (8p11) / SE 8 (D8Z1)	red/green	20	KBI-12754	VI
	ON FGFR1 (8p11) / SE 8 (D8Z1)	red/green	50	KBI-14754	VI
Sarcoma	ON COL1A1/PDGFB t(17;22) DC, S-Fusion	red/green	10	KBI-10742	VI
	ON EWSR1/NFATC2 t(20;22) DC, S-Fusion	red/green	10	KBI-10751	VII
Lymphoma (tissue)	ON MYC (8q24) Break, TC (tissue)	red/green/blue	10	KBI-10749	VII
	ON BCL2/IGH@ t(14;18) Fusion (tissue)	red/green	10	KBI-10755	VIII
MICRODELETION DNA PROBES					
	MD GATA4 (8p23) / SE 8	red/green	10	KBI-40118	VIII
	MD GATA4 (8p23) / SE 8	red/green	5	KBI-45118	VIII

ONCOLOGY - HEMATOLOGY DNA PROBES

	Description	Color	Tests	Cat#	Page
CML	ON FIP1L1-CHIC2-PDGFRA (4q12) Del, Break	red/green	10	KBI-10003	14
	ON PDGFRB (5q33) Break	red/green	10	KBI-10004	15
	ON BCR/ABL t(9;22) Fusion	red/green	10	KBI-10005	11,35
	ON BCR/ABL t(9;22) Fusion	red/green	20	KBI-12005	11,35
	ON BCR/ABL t(9;22) TC, D-Fusion	red/green/blue	10	KBI-10006	11,35
	ON FIP1L1-CHIC2-PDGFRA (4q12) Del, Break, TC	red/green/blue	10	KBI-10007	15
	ON BCR/ABL t(9;22,) DC, S-Fusion, ES	red/green	10	KBI-10008	12,35
	ON BCR/ABL t(9;22) DC, S-Fusion	red/green	10	KBI-10009	12,35
	ON p53 (17p13) / MPO (17q22) "ISO 17q"	green/red	10	KBI-10011	13
	ON JAK2 (9p24) Break	green/red	10	KBI-10012	13
CLL	ON DLEU (13q14) / 13qter	red/green	10	KBI-10102	17
	ON ATM (11q22) / SE 11	red/green	10	KBI-10103	18
	ON GLI (12q13) / SE 12	red/green	10	KBI-10104	20
	ON 6q21 / SE 6	red/green	10	KBI-10105	18
	ON C-MYC (8q24) / SE 8	red/green	10	KBI-10106	19
	ON ATM (11q22) / GLI (12q13)	red/green	10	KBI-10108	21
	ON 6q21 / MYC (8q24)	red/green	10	KBI-10117	21
	ON hTERC (3q26) / 3q11	red/green	10	KBI-10110	19
	ON p53 (17p13) / SE 17	red/green	10	KBI-10112	17
	ON p53 (17p13) / SE 17	red/green	20	KBI-12112	17
	ON DLEU (13q14) / p53 (17p13)	red/green	10	KBI-10113	20
	ON p53 (17p13) / ATM (11q22)	green/red	10	KBI-10114	22

	Description	Color	Tests	Cat#	Page
MDS	ON MDS 7q- (7q22; 7q36)	green/red	10	KBI-10202	25
	ON MDS 20q- (PTPRT 20q12) / 20q11	red/green	10	KBI-10203	26
	ON EVI t(3;3); inv(3) (3q26) Break	red/green	10	KBI-10204	26
	ON EVI t(3;3); inv(3) (3q26) Break, TC	red/green/blue	10	KBI-10205	27
	ON MDS 7q- (7q22; 7q36) / SE 7 TC	green/red/blue	10	KBI-10207	25
	ON hTERT (5p15) / 5q31	red/green	10	KBI-10208	23
	ON MDS 5q- (5q31; 5q33)	green/red	10	KBI-10209	24
	ON MDS 5q- (5q31; 5q33) / hTERT (5p15) TC	green/red/blue	10	KBI-10210	24
AML	ON AML/ETO t(8;21) Fusion	green/red	10	KBI-10301	28
	ON PML/RARA t(15;17) Fusion	green/red	10	KBI-10302	29
	ON PML/RARA t(15;17) Fusion	green/red	20	KBI-12302	29
	ON MLL (11q23) Break	red/green	10	KBI-10303	29,35
	ON CBFB t(16;16), inv(16) Break	red/green	10	KBI-10304	32
	ON RARA (17q21) Break	red/green	10	KBI-10305	31
	ON DEK / NUP214 t(6;9) Fusion	red/green	10	KBI-10306	32
	ON MLL/MLLT1 t(11;19) Fusion	red/green	10	KBI-10307	30
	ON MLL/MLLT3 t(9;11) Fusion	red/green	10	KBI-10308	30
	ON MLL/MLLT4 t(6;11) Fusion	red/green	10	KBI-10309	31
ALL	ON TEL/AML t(12;21) Fusion	red/green	10	KBI-10401	33
	ON p16 (9p21) / 9q21	red/green	10	KBI-10402	34
	ON ETV6 (TEL) (12p13) Break	red/green	10	KBI-10403	34
Multiple Myeloma	ON MM 11q23 / DLEU (13q14)	green/red	10	KBI-10502	38
	ON MM 1q21 / 8p21	green/red	10	KBI-10503	39
	ON MM 15q22 / 6q21	green/red	10	KBI-10504	40
	ON MM 1q21 / SRD (1p36)	green/red	10	KBI-10507	41
	ON MM 15q22 / 9q34	green/red	10	KBI-10508	40
	ON MM 19q13 / p53 (17p13)	green/red	10	KBI-10509	39
Lymphoma related probes	ON IGH (14q32) Break	red/green	10	KBI-10601	22,41,44
	ON FGFR3/IGH t(4;14) Fusion	green/red	10	KBI-10602	38,47
	ON MYC/IGH t(8;14) Fusion	green/red	10	KBI-10603	42
	ON BCL1/IGH t(11;14) Fusion	green/red	10	KBI-10604	43
	ON MYEOV/IGH t(11;14) Fusion	green/red	10	KBI-10605	36,47
	ON BCL2/IGH t(14;18) Fusion	green/red	10	KBI-10606	43
	ON BCL6 (3q27) Break	red/green	10	KBI-10607	45
	ON MALT (18q21) Break	red/green	10	KBI-10608	45
	ON CCND1 (BCL1;11q13) Break	red/green	10	KBI-10609	46
	ON MAF/IGH t(14;16) Fusion	green/red	10	KBI-10610	37
	ON MYC (8q24) Break, TC	red/green/blue	10	KBI-10611	47
	ON BCL2 (18q21) Break	red/green	10	KBI-10612	44

ONCOLOGY - SOLID TUMOR DNA PROBES

ON = Oncology probes

Description	Color	Tests	Cat#	Page
ON ERBB2, Her-2/Neu (17q12) / SE 17	red/green	10	KBI-10701	49
ON ERBB2, Her-2/Neu (17q12) / SE 17	red/green	50	KBI-14701	49
ON EGFR, Her-1 (7p11) / SE 7	red/green	10	KBI-10702	54
ON CC hTERC (3q26) C-MYC (8q24) / SE 7 TC	red/green/blue	10	KBI-10704	52
ON MYCN (2p24) / LAF (2q11)	red/green	10	KBI-10706	59
ON PPARγ (3p25) Break	red/green	10	KBI-10707	58
ON hTERT (5p15) / 5q31 (tissue)	red/green	10	KBI-10709	55
ON p16 (9p21) / 9q21 (tissue)	red/green	10	KBI-10710	52
ON MLL (11q23) / SE 11	red/green	10	KBI-10711	60
ON SRD (1p36) / SE 1(1qh)	red/green	10	KBI-10712	60
ON SYT (18q11) Break	red/green	10	KBI-10713	63
ON CHOP (12q13) Break	red/green	10	KBI-10714	63
ON FUS (16p11) Break	red/green	10	KBI-10715	64
ON FKHR (13q14) Break	red/green	10	KBI-10716	64
ON MDM2 (12q15) / SE 12	red/green	10	KBI-10717	65

Description	Color	Tests	Cat#	Page
ON PTEN (10q23) / SE 10	red/green	10	KBI-10718	57
ON C-MET (7q31) / SE 7	red/green	10	KBI-10719	55
ON AR (Xq12) / SE X	red/green	10	KBI-10720	56
ON AURKA (20q13) / 20q11	red/green	10	KBI-10721	67
ON AURKB (17p13) / SE 17	red/green	10	KBI-10722	68
ON TOP2A (17q21) / SE 17	red/green	10	KBI-10724	49
ON CDK4 (12q13) / SE 12	red/green	10	KBI-10725	66
ON TMPRSS2-ERG (21q22) Del, Break, TC	red/green/blue	10	KBI-10726	57
ON IGH (14q32) Break (tissue)	red/green	10	KBI-10729	70
ON BCL6 (3q27) Break (tissue)	red/green	10	KBI-10730	71
ON MALT (18q21) Break (tissue)	red/green	10	KBI-10731	71
ON ZNF217 (20q13) / 20q11	red/green	10	KBI-10733	50
ON CCND1 (11q13) / SE 11	red/green	10	KBI-10734	69
ON TOP2A (17q21) / Her-2/neu (17q12) / SE 17 TC	red/green/blue	10	KBI-10735	50
ON MDM4 (1q32) /SE 1	red/green	10	KBI-10736	61
ON FGFR1 (8p12) Break	red/green	10	KBI-10737	16,51
ON p53 (17p13) / SE 17 (tissue)	red/green	10	KBI-10738	72
ON ERCC1 (19q13) / ZNF443 (19p13)	red/green	10	KBI-10739	66
ON TFE3 (Xp11) Break	red/green	10	KBI-10741	72
ON BCL2 (18q21) Break (tissue)	red/green	10	KBI-10745	70
ON ALK/EML4 t(2;2); inv(2) Fusion	red/green	10	KBI-10746	54
ON ALK (2p23) Break	red/green	10	KBI-10747	53,73
ON EWSR1 (22q12) Break	red/green	10	KBI-10750	62

ONCOLOGY - CHROMOGENIC IN SITU HYBRIDIZATION

Description	Tests	Cat#	Page
UniStar CISH Detection Kit	10	KBI-50001	74
UniStar Her2/neu (17q12)	10	KBI-50701	74
UniStar EGFR (7p11)	10	KBI-50702	74
UniStar C-MET (7q31)	10	KBI-50719	74
TwinStar CISH Detection Kit	10	KBI-60010	74
TwinStar Her2/neu (17q12)	10	KBI-60701	74
TwinStar EGFR (7p11)	10	KBI-60702	74
TwinStar C-MET (7q31)	10	KBI-60719	74

PREIMPLANTATION GENETIC SCREENING

Description	Color	Tests	Cat#	Page
PreimpScreen PolB (13,16,18,21,22)	five color	20	KBI-40050	77
PreimpScreen Blas (13,18,21,X,Y)	five color	20	KBI-40051	77
MultiStar 24 FISH	six color, 4 panels	10	KBI-40060	77
MultiStar FISH Panel 1	six color	10	KBI-40061	77
MultiStar FISH Panel 2	six color	10	KBI-40062	77
MultiStar FISH Panel 3	six color	10	KBI-40063	77
MultiStar FISH Panel 4	six color	10	KBI-40064	77

PRENATAL DNA PROBES

PN = Prenatal probes

Description	*Color*	*Tests*	*Cat#*	*Page*
PN 13 (13q14)	green	10	KBI-40001	78
PN 21 (21q22)	red	10	KBI-40002	78
PN 13 (13q14) / 21 (21q22)	green/red	10	KBI-40003	79
SE 18 (D18Z1) 5x conc	blue	10	KBI-20018-B	79
SE X (DXZ1) / SE Y (DYZ3)	green/red	10	KBI-20030	79
SE 7 (D7Z1) / SE 8 (D8Z1)	red/green	10	KBI-20031	79
SE (X,Y,18)	green/red/blue	10	KBI-20032	79
PrenatScreen (13/21, X/Y18)	green/red/blue	10	KBI-40005	79
PrenatScreen (13/21, X/Y18)	green/red/blue	30	KBI-40006	79
PrenatScreen (13/21, X/Y18)	green/red/blue	50	KBI-40007	79
PloidyScreen (21, X, Y)	red/green/blue	20	KBI-40008	79

MICRODELETION DNA PROBES

MD = Microdeletion probes

Description	*Color*	*Tests*	*Cat#*	*Page*
MD Miller-Dieker LIS (17p13) / Smith-Magenis RAI (17p11)	red/green	10	KBI-40101	87
MD DiGeorge "N25" (22q11) / 22q13 (SHANK3)	red/green	10	KBI-40102	81,83
MD DiGeorge Tuple (22q11) / 22q13 (SHANK3)	red/green	10	KBI-40103	81,83
MD DiGeorge T-box1 (22q11) / 22q13 (SHANK3)	red/green	10	KBI-40104	82,83
MD DiGeorge II (10p14) / SE 10	red/green	10	KBI-40105	83
MD Cri-Du-Chat CTNND (5p15) / 5q31	red/green	10	KBI-40106	88
MD Wolf-Hirschhorn WHSC1 (4p16) / SE 4	red/green	10	KBI-40107	88
MD X-Inactivation XIST (Xq13) / SE X	red/green	10	KBI-40108	89
MD Prader-Willi SNRPN (15q11) / PML(15q24)	red/green	10	KBI-40109	85
MD Angelman UBE3A (15q11) / PML(15q24)	red/green	10	KBI-40110	86
MD Williams-Beuren ELN (7q11) / 7q22	red/green	10	KBI-40111	86
MD Short Stature (Xp22) / SE X	red/green	10	KBI-40112	89
MD NSD1 (5q35)/ hTERT (5p15)	red/green	10	KBI-40113	84
MD NF1 (17q11) / MPO (17q22)	red/green	10	KBI-40114	84
MD STS (Xp22) / KAL (Xp22) / SE X TC	red/green/blue	10	KBI-40115	90
MD IGF1R (15q26) / 15q11	red/green	10	KBI-40116	91

SATELLITE ENUMERATION DNA PROBES

SE = Satellite Enumeration probes
5x conc format

Description	*Color*	*Tests*	*Cat#*	*Page*
All Human Centromer (AHC), RTU	green or red	10	KBI-20000	94
SE 1 (1qh)	green, red, or blue	10	KBI-20001	94
SE 2 (D2Z)	green, red, or blue	10	KBI-20002	94
SE 3 (D3Z1)	green, red, or blue	10	KBI-20003	94
SE 4 (D4Z1)	green, red, or blue	10	KBI-20004	94
SE 6 (D6Z1)	green, red, or blue	10	KBI-20006	94
SE 7 (D7Z1)	green, red, or blue	10	KBI-20007	94
SE 8 (D8Z1)	green, red, or blue	10	KBI-20008	14,94
SE 9 (classical)	green, red, or blue	10	KBI-20009	94
SE 10 (D10Z1)	green, red, or blue	10	KBI-20010	94
SE 11 (D11Z1)	green, red, or blue	10	KBI-20011	94
SE 12 (D12Z3)	green, red, or blue	10	KBI-20012	22,94
SE 15 (D15Z)	green, red, or blue	10	KBI-20015	94
SE 16 (D16Z2)	green, red, or blue	10	KBI-20016	94
SE 17 (D17Z1)	green, red, or blue	10	KBI-20017	94
SE 18 (D18Z1)	green, red, or blue	10	KBI-20018	94
SE 20 (D20Z1)	green, red, or blue	10	KBI-20020	94
SE X (DXZ1)	green, red, or blue	10	KBI-20023	94
SE Y (DYZ3)	green, red, or blue	10	KBI-20024	94
SE Y classical q arm	green, red, or blue	10	KBI-20025	94
SE 1/5/19	green, red, or blue	10	KBI-20026	94
SE 13/21	green, red, or blue	10	KBI-20027	94
SE 14/22	green, red, or blue	10	KBI-20028	94
SE X (DXZ1) / SE Y (DYZ3)	green/red	10	KBI-20030	94
SE 7 (D7Z1) / SE 8 (D8Z1)	red/green	10	KBI-20031	14,94
SE (X,Y,18)	green/red/blue	10	KBI-20032	94
Acro-P-Arms NOR	green, red, or blue	10	KBI-20033	95

* Add -G for Green, -R for Red, -B for Blue (available on request)

SUB-TELOMERE DNA PROBES

5x conc format

Description	*Color*	*Tests*	*Cat#*	*Page*
Sub Telomere 1pter	green, red, or blue	5	KBI-40201	92
Sub Telomere 1qter	green, red, or blue	5	KBI-40202	92
Sub Telomere 2pter	green, red, or blue	5	KBI-40203	92
Sub Telomere 2qter	green, red, or blue	5	KBI-40204	92
Sub Telomere 3pter	green, red, or blue	5	KBI-40205	92
Sub Telomere 3qter	green, red, or blue	5	KBI-40206	92
Sub Telomere 4pter	green, red, or blue	5	KBI-40207	92
Sub Telomere 4qter	green, red, or blue	5	KBI-40208	92
Sub Telomere 5pter	green, red, or blue	5	KBI-40209	92
Sub Telomere 5qter	green, red, or blue	5	KBI-40210	92
Sub Telomere 6pter	green, red, or blue	5	KBI-40211	92
Sub Telomere 6qter	green, red, or blue	5	KBI-40212	92
Sub Telomere 7pter	green, red, or blue	5	KBI-40213	92
Sub Telomere 7qter	green, red, or blue	5	KBI-40214	92
Sub Telomere 8pter	green, red, or blue	5	KBI-40215	92
Sub Telomere 8qter	green, red, or blue	5	KBI-40216	92
Sub Telomere 9pter	green, red, or blue	5	KBI-40217	92
Sub Telomere 9qter	green, red, or blue	5	KBI-40218	92
Sub Telomere 10pter	green, red, or blue	5	KBI-40219	92
Sub Telomere 10qter	green, red, or blue	5	KBI-40220	92
Sub Telomere 11pter	green, red, or blue	5	KBI-40221	92
Sub Telomere 11qter	green, red, or blue	5	KBI-40222	92
Sub Telomere 12pter	green, red, or blue	5	KBI-40223	92
Sub Telomere 12qter	green, red, or blue	5	KBI-40224	92
Sub Telomere 13qter	green, red, or blue	5	KBI-40225	92
Sub Telomere 14qter	green, red, or blue	5	KBI-40226	92
Sub Telomere 15qter	green, red, or blue	5	KBI-40227	92
Sub Telomere 16pter	green, red, or blue	5	KBI-40228	92
Sub Telomere 16qter	green, red, or blue	5	KBI-40229	92
Sub Telomere 17pter	green, red, or blue	5	KBI-40230	92
Sub Telomere 17qter	green, red, or blue	5	KBI-40231	92
Sub Telomere 18pter	green, red, or blue	5	KBI-40232	92
Sub Telomere 18qter	green, red, or blue	5	KBI-40233	92
Sub Telomere 19pter	green, red, or blue	5	KBI-40234	92
Sub Telomere 19qter	green, red, or blue	5	KBI-40235	92
Sub Telomere 20pter	green, red, or blue	5	KBI-40236	92
Sub Telomere 20qter	green, red, or blue	5	KBI-40237	92
Sub Telomere 21qter	green, red, or blue	5	KBI-40238	92
Sub Telomere 22qter	green, red, or blue	5	KBI-40239	92
Sub Telomere XYpter	green, red, or blue	5	KBI-40240	92
Sub Telomere XYqter	green, red, or blue	5	KBI-40241	92

* Add -G for Green, -R for Red, -B for Blue (available on request)

ARM SPECIFIC / BAND SPECIFIC DNA PROBES

ready-to-use

Description	*Color*	*Tests*	*Cat#*	*Page*
Arm Specific Probe 1p	green or red	5	KBI-30100	99
Arm Specific Probe 1q	green or red	5	KBI-30101	99
Arm Specific Probe 2p	green or red	5	KBI-30102	99
Arm Specific Probe 2q	green or red	5	KBI-30103	99
Arm Specific Probe 3p	green or red	5	KBI-30104	99
Arm Specific Probe 3q	green or red	5	KBI-30105	99
Arm Specific Probe 4p	green or red	5	KBI-30106	99
Arm Specific Probe 4q	green or red	5	KBI-30107	99
Arm Specific Probe 5p	green or red	5	KBI-30108	99
Arm Specific Probe 5q	green or red	5	KBI-30109	99
Arm Specific Probe 6p	green or red	5	KBI-30110	99
Arm Specific Probe 6q	green or red	5	KBI-30111	99
Arm Specific Probe 7p	green or red	5	KBI-30112	99
Arm Specific Probe 7q	green or red	5	KBI-30113	99
Arm Specific Probe 8p	green or red	5	KBI-30114	99
Arm Specific Probe 8q	green or red	5	KBI-30115	99
Arm Specific Probe 9p	green or red	5	KBI-30116	99
Arm Specific Probe 9q	green or red	5	KBI-30117	99
Arm Specific Probe 10p	green or red	5	KBI-30118	99
Arm Specific Probe 10q	green or red	5	KBI-30119	99
Arm Specific Probe 11p	green or red	5	KBI-30120	99
Arm Specific Probe 11q	green or red	5	KBI-30121	99
Arm Specific Probe 12p	green or red	5	KBI-30122	99
Arm Specific Probe 12q	green or red	5	KBI-30123	99
Arm Specific Probe 13q	green or red	5	KBI-30124	99
Arm Specific Probe 14q	green or red	5	KBI-30125	99
Arm Specific Probe 15q	green or red	5	KBI-30126	99
Arm Specific Probe 16p	green or red	5	KBI-30127	99
Arm Specific Probe 16q	green or red	5	KBI-30128	99
Arm Specific Probe 17p	green or red	5	KBI-30129	99
Arm Specific Probe 17q	green or red	5	KBI-30130	99
Arm Specific Probe 18p	green or red	5	KBI-30131	99
Arm Specific Probe 18q	green or red	5	KBI-30132	99
Arm Specific Probe 19p	green or red	5	KBI-30133	99
Arm Specific Probe 19q	green or red	5	KBI-30134	99
Arm Specific Probe 20p	green or red	5	KBI-30135	99
Arm Specific Probe 20q	green or red	5	KBI-30136	99
Arm Specific Probe 21q	green or red	5	KBI-30137	99
Arm Specific Probe 22q	green or red	5	KBI-30138	99
Arm Specific Probe Xp	green or red	5	KBI-30139	99
Arm Specific Probe Xq	green or red	5	KBI-30140	99
Arm Specific Probe Yq	green or red	5	KBI-30141	99
Band Specific Probes - inquire	green or red	20	KBI-302xx	99

*Add -G for Green, -R for Red

WHOLE CHROMOSOME DNA PROBES

5x conc format

Description	Color	Tests	Cat#	Page
Whole Chromosome 1	green, red, or blue	5	KBI-30001	97
Whole Chromosome 2	green, red, or blue	5	KBI-30002	97
Whole Chromosome 3	green, red, or blue	5	KBI-30003	97
Whole Chromosome 4	green, red, or blue	5	KBI-30004	97
Whole Chromosome 5	green, red, or blue	5	KBI-30005	97
Whole Chromosome 6	green, red, or blue	5	KBI-30006	97
Whole Chromosome 7	green, red, or blue	5	KBI-30007	97
Whole Chromosome 8	green, red, or blue	5	KBI-30008	97
Whole Chromosome 9	green, red, or blue	5	KBI-30009	97
Whole Chromosome 10	green, red, or blue	5	KBI-30010	97
Whole Chromosome 11	green, red, or blue	5	KBI-30011	97
Whole Chromosome 12	green, red, or blue	5	KBI-30012	97
Whole Chromosome 13	green, red, or blue	5	KBI-30013	97
Whole Chromosome 14	green, red, or blue	5	KBI-30014	97
Whole Chromosome 15	green, red, or blue	5	KBI-30015	97
Whole Chromosome 16	green, red, or blue	5	KBI-30016	97
Whole Chromosome 17	green, red, or blue	5	KBI-30017	97
Whole Chromosome 18	green, red, or blue	5	KBI-30018	97
Whole Chromosome 19	green, red, or blue	5	KBI-30019	97
Whole Chromosome 20	green, red, or blue	5	KBI-30020	97
Whole Chromosome 21	green, red, or blue	5	KBI-30021	97
Whole Chromosome 22	green, red, or blue	5	KBI-30022	97
Whole Chromosome X	green, red, or blue	5	KBI-30023	97
Whole Chromosome Y	green, red, or blue	5	KBI-30024	97

* Add -G for Green, -R for Red, -B for Blue (available on request)

MOUSE DNA PROBES

Description	Color	Tests	Cat#	Page
All Mouse Centromere (AMC)	red or green	10	KBI-30500	100
TK (11qE1) / AurKa (2qH3)	red/green	10	KBI-30501	100
TK (11qE1) / WC Y	red/green	10	KBI-30502	100
RAB9B (XqF1) / DSCR (16qC4)	red/green	10	KBI-30503	100
RAB9B (XqF1) / WC Y	red/green	10	KBI-30505	100

* Add -G for Green, -R for Red

CELL CULTURE MEDIA / ACCESSORIES

Description	*Contents*	*Cat#*	*Page*
KREA*vital* Prenatal Medium (Basal)	90ml	KBI-90010	102
KREA*vital* Prenatal Medium (Basal)	450ml	KBI-92010	102
KREA*vital* Prenatal Medium (Supplement)	10ml	KBI-90011	102
KREA*vital* Prenatal Medium (Supplement)	50ml	KBI-92011	102
KREA*vital* Prenatal Medium (Complete)	100ml	KBI-90012	102
KREA*vital* Prenatal Medium (Complete)	500ml	KBI-92012	102
KREA*vital* Prenatal Medium PLUS (Complete)	100ml	KBI-90013	102
KREA*vital* Prenatal Medium PLUS (Complete)	500ml	KBI-92013	102
KREA*vital* Lymphocyte Karyotyping Medium (without PHA)	100ml	KBI-90020	102
KREA*vital* Lymphocyte Karyotyping Medium (without PHA)	500ml	KBI-92020	102
KREA*vital* Lymphocyte Karyotyping Medium (including PHA)	100ml	KBI-90021	102
KREA*vital* Lymphocyte Karyotyping Medium (including PHA)	500ml	KBI-92021	102
KREA*vital* Bone Marrow Karyotyping Medium	100ml	KBI-90030	102
KREA*vital* Bone Marrow Karyotyping Medium	500ml	KBI-92030	102
KREA*vital* Myeloid Cell Medium	100ml	KBI-90031	102
KREA*vital* Myeloid Cell Medium	500ml	KBI-92031	102
Colchicine Solution (10µg/ml, in PBS)	25ml	KBI-90050	102
Colcemid Solution (10µg/ml, in PBS)	10ml	KBI-90051	102
Potassium Chloride (0.075M)	100ml	KBI-90052	102
Phytohaemagglutinin M-Form	5ml	KBI-90053	102
Sodium Citrate Solution (0.8%)	500ml	KBI-90054	102
Trypsin EDTA 10X (EDTA 0.2%, Trypsin 0.5%, in saline solution)	20ml	KBI-90055	102
Trypsin EDTA 10X (EDTA 0.2%, Trypsin 0.5%, in saline solution)	100ml	KBI-92055	102

PRETREATMENT KITS / REAGENTS

Description	*Contents*	*Cat#*	*Page*
POSEIDON™ Tissue Digestion Kit II	5x5 slides	KBI-60004	103
POSEIDON FISH Reagent Kit	5x5 slides	KBI-60005	103
POSEIDON FISH Digestion Kit	5x5 slides	KBI-60006	103
POSEIDON Tissue Digestion Kit I	5x5 slides	KBI-60007	103
Rubber Cement, Fixogum	125 ml	LK-071A	103
DAPI Counterstain (0.1µg/ml)	1 ml	LK-095A	103
DAPI Counterstain (1µg/ml)	1 ml	LK-096A	103
Counterstain Diluent	1 ml	LK-097A	103
Pepsin Solution	2.5 ml	LK-101A	103
Wash Buffer I (0.4 x SSC/0.3% Igepal)	100 ml	LK-102A	103
Wash Buffer II (2 x SSC/0.1% Igepal)	100 ml	LK-103A	103
FISH Hybridization Buffer (FHB)	100 µl	KBI-FHB	103
Paraffin Tissue Buffer (PTB)	100 µl	KBI-PTB	103
Whole Chromosome Buffer (WCB)	50 µl	KBI-WCB	103

EQUIPMENT

Description	*Contents*	*Cat#*	*Page*
ThermoBrite™ (240V, 50 - 60Hz)		TS-02	104
Humidity Control Cards	10	HC-10	104
Cytofuge®2 (100 - 240V, 50 / 60 Hz)		CF-02	104

ARRAYCGH

Description	*Reactions*	*Cat#*	*Page*
ULS™ arrayCGH Labeling Kit (with Cy3 and Cy5)	for labeling 2 x 20 µg DNA	EA-005	107
ULS arrayCGH Labeling Kit (with Cy3)	for labeling 40 µg DNA	EA-005A	107
ULS arrayCGH Labeling Kit (with Cy5)	for labeling 40 µg DNA	EA-005B	107

DNA PRODUCTS

Description	*Reactions*	*Cat#*	*Page*
Array-Grade KREA*cot* DNA	500 µg	EA-020	108
Array-Grade KREA*cot* DNA	10 mg	EA-035	108
Megapool Reference DNA, male	200 µg	EA-100M	108
Megapool Reference DNA, female	200 µg	EA-100F	108

GENE EXPRESSION

Description	*Reactions*	*Cat#*	*Page*
ULS aRNA Labeling Kit (with Cy3 and Cy5)	for labeling 2 x 50 µg aRNA	EA-006	109
ULS aRNA Labeling Kit (with Biotin for Affymetrix® Genechips®)	for labeling 500 µg aRNA	EA-010	109
ULS aRNA Labeling Kit (with Biotin)	for labeling 250 µg aRNA	EA-018	109
ULS Fluorescent Labeling Kit for Agilent arrays (with Cy3 and Cy5)	for labeling 2 x 50 µg aRNA	EA-021	109
ULS Fluorescent Labeling Kit for Agilent arrays (with Cy5)	for labeling 50 µg aRNA	EA-022	109
ULS Fluorescent Labeling Kit for Agilent arrays (with Cy3)	for labeling 50 µg aRNA	EA-023	109
ULS Labeling Kit for CombiMatrix arrays (with Cy5)	for labeling 125 µg aRNA	EA-025	109
ULS Labeling Kit for CombiMatrix arrays (with Biotin)	for labeling 125 µg aRNA	EA-027	109
(20 amplifications each)			

MICRO RNA

Description	*Reactions*	*Cat#*	*Page*
ULS™ microRNA Labeling Kit (with Cy3 and Cy5)	for labeling 2 x 25 µg RNA	EA-036	110
ULS microRNA Labeling Kit (with Cy3)	for labeling 50 µg RNA	EA-037	110
ULS microRNA Labeling Kit (with Cy5)	for labeling 50 µg RNA	EA-038	110

GENERAL NUCLEIC ACID LABELING

Description	*Reactions*	*Cat#*	*Page*
Platinum*Bright*™ Nucleic Acid Labeling Kit (495 Green)	for labeling 20 µg template	GLK-001	111
Platinum*Bright* Nucleic Acid Labeling Kit (547 Light Red)	for labeling 20 µg template	GLK-002	111
Platinum*Bright* Nucleic Acid Labeling Kit (647 Far Red)	for labeling 20 µg template	GLK-003	111
Platinum*Bright* Nucleic Acid Labeling Kit (550 Red)	for labeling 20 µg template	GLK-004	111
Platinum*Bright* Nucleic Acid Labeling Kit (415 Blue)	for labeling 20 µg template	GLK-006	111
Platinum*Bright* Nucleic Acid Labeling Kit (Biotin)	for labeling 20 µg template	GLK-007	111
FISH*Bright*™ 415 Blue	for labeling 10 µg DNA	FLK-001	111
FISH*Bright* 495 Green	for labeling 10 µg DNA	FLK-002	111
FISH*Bright* 505 Green	for labeling 10 µg DNA	FLK-003	111
FISH*Bright* 550 Red	for labeling 10 µg DNA	FLK-004	111
FISH*Bright* 547 Light Red	for labeling 10 µg DNA	FLK-005	111
FISH*Bright* 647 Far Red	for labeling 10 µg DNA	FLK-006	111
FISH*Bright* Biotin	for labeling 10 µg DNA	FLK-007	111
FISH Grade CoT	500 µg	KB-COT	112

PROTEIN LABELING / **ANTIBODY** LABELING

Description	*Reactions*	*Cat#*	*Page*
Platinum*Link* Protein Labeling Kit (BIO)	4 single labelings	PLK-007	113
Platinum*Link* Protein Labeling Kit (FLU)	4 single labelings	PLK-009	113
Platinum*Link* Protein Labeling Kit (RHO)	4 single labelings	PLK-010	113

SUPPORTING PRODUCTS

Description	*Reactions*	*Cat#*	*Page*
KREA*pure*™ columns	20 pcs	KP-020	114
KREA*pure* columns	50 pcs	KP-050	114
KREA*pure* 96	1 plate	KP-096	114

CE MARKING & ISO CERTIFICATES

All probes from KREATECH are manufactured and marketed in accordance with the European IVD Directive 98/79/EC. Apart from those products designed for research use (Kreatech´s ASP, BSP, and mouse FISH probes, as well as the ULS™ Labeling product line), all KREATECH products are CE marked. In addition, KREATECH has obtained certificates for CE-marking of conformity for our prenatal and preimplantation genetic screening probes.

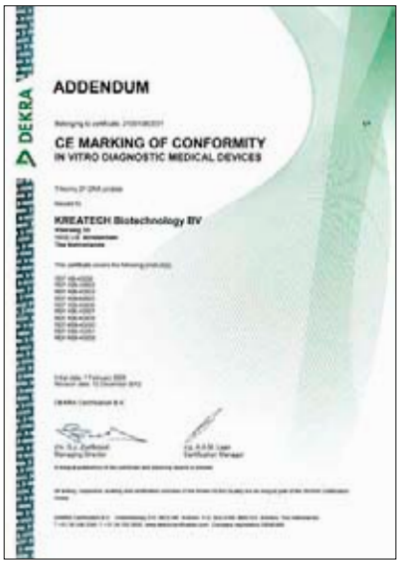
CE

All CE-marked FISH probes in this catalog are manufactured at KREATECH Diagnostics facilities in Amsterdam, The Netherlands, and are labeled with ULS (Universal Linkage System).

Manufacturing of all CE-marked products by KREATECH is carried out according to international standards ISO 9001:2008 and ISO 13485:2003 for which KREATECH holds certificates.

Compliance to the European IVD Directive 98/79/EC, ISO 9001:2008 and ISO 13485:2003 means that we are providing high quality in vitro diagnostic medical devices to be used for diagnosis, prevention, monitoring, treatment, alleviation or investigation of disease, congenital disorders, physiological and/or pathological state of the human body without being used in or on the human body.

We strive to continuously improve the quality of these products based on the latest developments and techniques.



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HUGO GENE SYMBOLS

The table below gives the approved HUGO Gene Symbol and synonyms used for the genes in our REPEAT-FREE™ POSEIDON™ probes according to the HUGO Gene Nomenclature Committee (HGNC).

Chromosome position	*Genes involved*	*HUGO Gene Symbols*	*Synonyms*	*Cat.# KBI*	*Page*
1p36	CHD5	CHD5		10507	41
				10712	60
1q21	S100A10	S100A10	42C, "annexin II tetramer (AIIt) p11 subunit", CLP11, P11	10503	39
				10507	41
1q32	MDM4	MDM4	MDMX	10736	61
2p21	EML4	EML4	ELP120, ROPP120	10746	54
2p23	ALK	ALK	CD246	10746	54
				10747	53,73
2p24	MYCN	MYCN	bHLHe37, N-myc	10706	59
2q11	LAF	AFF3	MLLT2-like	10706	59
3p25	PPARγ	PPARG	PPARG1, PPARG2, NR1C3, PPARgamma	10707	58
3q26	EVI	MECOM	MDS1-EVI1, PRDM3	10204	26
				10205	27
3q26	hTERC	TERC	hTR, SCARNA19, "small Cajal body-specific RNA 19", TR, TRC3	10110	19
				10204	26
				10205	27
				10704	52
3q27	BCL6	BCL6	BCL5, BCL6A, LAZ3, ZBTB27	10607	45
				10730	71
4p16	FGFR3	FGFR3	CD333, CEK2, JTK4	10602	38,47
4p16	WHSC1	WHSC1	MMSET, NSD2	40107	88
4q12	CHIC2	CHIC2	BTL	10003	14
				10007	15
4q12	FIP1L1	FIP1L1	DKFZp586K0717	10003	14
				10007	15
4q12	PDGFRA	PDGFRA	CD140a, PDGFR2	10003	14
				10007	15
4q21-22	AFF1	AFF1	AF-4, AF4	10404	III
5p15	CTNND	CTNND2	GT24, "neural plakophilin-related arm-repeat protein", NPRAP	40106	88
5p15	hTERT	TERT	EST2, hEST2, TCS1, TP2, TRT	10208	23
				10210	24
				10709	55
				40113	84
5q31	CDC25C	CDC25C	PPP1R60, "protein phosphatase 1, regulatory subunit 60"	10208	23
				10209	24
				10210	24
				10709	55
5q31	EGR1	EGR1	TIS8, G0S30, NGFI-A, KROX-24, ZIF-268, AT225, ZNF225	10208	23
				10209	24
				10210	24
				10709	55
5q33	CSF1R	CSF1R	C-FMS, CD115, CSFR	10209	24
				10210	24
5q33	PDGFRB	PDGFRB	CD140b, JTK12, PDGFR1	10004	15
				40064	77
5q33	RPS14	RPS14	"40S ribosomal protein S14", "emetine resistance", EMTB, S14	10209	24
				10210	24
5q35	NSD1	NSD1	ARA267, FLJ22263, KMT3B	40113	84
6p22	DEK	DEK	D6S231E	10306	32
6q21	SEC63	SEC63	DNAJC23, ERdj2, PRO2507, SEC63L	10105	18
				10117	21
				10504	40
6q22	ROS1	ROS1	c-ros-1, MCF3, ROS	10752	V
6q27	MLLT4	MLLT4	AF-6, AF6	10309	31
7p11	EGFR, Her1	EGFR	ERBB1	10702	54
7q11	ELN	ELN	"supravalvular aortic stenosis", SVAS, "tropoelastin", WBS, "Williams-Beuren syndrome", WS	40111	86
7q11	LIMK1	LIMK1	LIMK	40111	86
7q22	CUTL1	CUX1	CASP, CDP, CDP/Cut, CDP/Cux, CDP1, Clox, CUT, CUX, Cux/CDP, ""golgi integral membrane protein 6"", GOLIM6"	10202	25
				10207	25
7q31	C-MET	MET	HGFR, RCCP2	10719	55
8p11	FGFR1	FGFR1	BFGFR, BFGFR, CD331, CEK, FLG, H2, H3, H4, H5, N-SAM, "Pfeiffer syndrome"	12754	VI
				14754	VI
				10737	16,51
8p21	PNOC	PNOC	"nocistatin", PPNOC	10503	39
8p23	GATA4	GATA4		40118	VII

Chromosome position	*Genes involved*	*HUGO Gene Symbols*	*Synonyms*	*Cat.# KBI*	*Page*
8p21	ETO	RUNX1T	CDR, ETO, MTG8, ZMYND2	10301	28
8q24	C-MYC	MYC	bHLHe39, c-Myc	10106	19
				10117	21
				10603	42
				10611	47
				10704	52
9p21	p16	CDKN2A	CDK4I, p16, INK4a, MTS1, CMM2, ARF, p19, p14, INK4, p16INK4a, p19Arf	10402	34
				10710	52
9p21	MLLT3	MLLT3	AF-9, AF9, YEATS3	10308	30
9p24	JAK2	JAK2	JTK10	10012	13
9q34	ABL	ABL1	JTK7, c-ABL, p150	10005	11,35
				10006	11,35
				10008	12,35
				10009	12,35
				10013	II
9q34	ASS	ASS1	CTLN1	10005	11,35
				10006	11,35
				10008	12,35
				10013	II
				10508	40
9q34	NUP214	NUP214	CAIN, CAN, "CAN protein, putative oncogene", D9S46E, N214, "nuclear pore complex protein Nup214"	10306	32
10q11	RET	RET	"cadherin-related family member 16", CDHF12, CDHR16, PTC, RET51	10753	V
10q23	PTEN	PTEN	MMAC1, "mutated in multiple advanced cancers 1", PTEN1, TEP1	10718	57
11p15	NUP98	NUP98	NUP96	10311	III
11q13	BCL1	CCND1	"B-cell CLL/lymphoma 1", "G1/S-specific cyclin D1", "parathyroid adenomatosis 1", U21B31	10604	43
				10605	36,57
				10609	46
				10734	69
11q13	MYEOV	MYEOV	OCIM	10605	36,47
11q22	ATM	ATM	TEL1, "TEL1, telomere maintenance 1, homolog (S. cerevisiae)", TELO1	10103	18
				10108	21
				10114	22
11q23	MLL	MLL	ALL-1, CXXC7, HRX, HTRX1, KMT2A, MLL1A, TRX1	10303	29,35
				10307	30
				10308	30
				10309	31
				10404	III
				10711	60
11q23	PLZF	ZBTB16	PLZF	10502	38
12p13	TEL	ETV6	TEL, "TEL oncogene"	10401	33
				10403	34
12q13	CDK4	CDK4	PSK-J3	10725	66
12q13	CHOP	DDIT3	""C/EBP zeta"", CHOP, CHOP10, GADD153"	10714	63
12q13	GLI	GLI1		10104	20
				10108	21
12q15	MDM2	MDM2	HDM2, HDMX, MGC5370	10717	65
13q14	DLEU	DLEU1	"B-cell neoplasia-associated gene with multiple splicing", LEU1, LINC00021, "long intergenic non-protein coding RNA 21", NCRNA00021, "non-protein coding RNA 21", XTP6	10102	17
				10113	20
				10502	38
13q14	FKHR	FOXO1	FKH1	10716	64
13q14	RB7	RB1	RB	40001	78
				40003	79
				40005	79
				40050	77
				40051	77
				40064	77
14q32	IGH	IGH@	IGH	10510	IV
				10601	22,41,44
				10602	38,47
				10603	42
				10604	43
				10605	36,47
				10606	43
				10610	37
				10729	70
				10755	VIII

Chromosome position	Genes involved	HUGO Gene Symbols	Synonyms	Cat.# KBI	Page
15q11	SNRPN	SNRPN	HCERN3, RT-LI, "SM protein N", SM-D, "small nuclear ribonucleoprotein N", SMN, SNRNP-N, SNURF-SNRPN, "tissue-specific splicing protein"	40109	85
15q11	UBE3A	UBE3A	hUba3, "UBA3, ubiquitin-activating enzyme E1 homolog (yeast)"	40110	86
				40116	91
15q22	SMAD6	SMAD6	HsT17432	10504	40
				10508	40
15q24	PML	PML	MYL, RNF71, TRIM19"	10302	29
				40109	85
				40110	86
15q26	IGF1R	IGF1R	CD221, IGFIR, IGFR, JTK13, MGC18216	40116	91
16p11	FUS	FUS	FUS1, "heterogeneous nuclear ribonucleoprotein P2", hnRNP-P2, TLS, "translocated in liposarcoma"	10715	64
16q22	CBFB	CBFB	PEBP2B	10304	32,35
16q23	MAF	MAF	c-MAF	10610	37
17p11	RAI1	RAI1	DKFZP434A139, KIAA1820, MGC12824, SMS	40101	87
17p13	AURKB	AURKB	Aik2, AIM-1, ARK2, AurB, "aurora-1", "aurora-B", IPL1, PPP1R48, "protein phosphatase 1, regulatory subunit 48", STK5	10722	68
17p13	LIS	PAFAH1B1	LIS1, PAFAH	40101	87
17p13	p53	TP53	LFS1, "Li-Fraumeni syndrome", p53	10011	13
				10112	17
				10113	20
				10114	22
				10509	39
				10738	72
17q11	NF1	NF1	"neurofibromatosis", "von Recklinghausen disease", "Watson disease"	40114	84
17q12	ERBB2	ERBB2	CD340, HER-2, HER2, NEU	10701	49
				10735	50
17q21	COL1A1	COL1A1	OI4	10742	VI
17q21	RARA	RARA	NR1B1, RAR	10302	29
				10305	31
17q21	TOP2A	TOP2A		10724	49
				10735	50
17q22	MPO	MPO		10011	13
				40114	84
18q11	SYT	SS18	SYT	10713	63
18q21	BCL2	BCL2	Bcl-2, PPP1R50, "protein phosphatase 1, regulatory subunit 50"	10606	43
				10612	44
				10745	70
				10755	VIII
18q21	MALT	MALT1	"paracaspase"	10608	45
				10731	71
19p13	MLLT1	MLLT1	ENL, LTG19, YEATS1	10307	30
19p13	ZNF443	ZNF443	ZK1	10739	66
19q13	CD37	CD37	TSPAN26	10509	39
				40064	77
19q13	ERCC1	ERCC1	RAD10	10739	66
20q11	MAPRE1	MAPRE1	"adenomatous polyposis coli-binding protein EB1", EB1	10203	26
				10721	67
				10733	50
20q12	MAFB	MAFB	""Kreisler (mouse) maf-related leucine zipper homolog"", KR"	10510	IV
20q12	PTPRT	PTPRT	KIAA0283, RPTPrho	10203	26
20q13	AURKA	AURKA	AIK, ARK1, AurA, "Aurora-A kinase", BTAK, PPP1R47, "protein phosphatase 1, regulatory subunit 47", STK7	10721	67
20q13	NFATC2	NFATC2	NF-ATP, NFAT1, NFATp	10751	VII
20q13	ZNF217	ZNF217	ZABC1	10733	50
21q22	AML	RUNX1	"aml1 oncogene", AMLCR1, PEBP2A2	10301	28
21q22	DSCR1	RCAN1		40002	79
				40003	79
				40005	79
				40006	79
				40007	79
				40008	79
				40050	77
				40051	77
21q22	ERG	ERG	erg-3, p55, "TMPRSS2-ERG prostate cancer specific", "transcriptional regulator ERG (transforming protein ERG)", "v-ets avian erythroblastosis virus E26 oncogene related", "v-ets erythroblastosis virus E26 oncogene like"	10726	57

Chromosome position	*Genes involved*	*HUGO Gene Symbols*	*Synonyms*	*Cat.# KBI*	*Page*
21q22	TMPRSS2	TMPRSS2	PRSS10	10726	57
22q11	BCR	BCR	ALL, CML, D22S662, PHL	10005	11,35
				10006	11,35
				10008	12,35
				10009	12,35
				10013	II
22q11	CLH22	CLTCL1	CHC22, CLH22, CLTD	40102	81,83
22q11	DGCR2	DGCR2	DGS-C, IDD, "integral membrane protein DGCR2", KIAA0163, LAN, SEZ-12	40102	81,83
22q11	TUPLE	HIRA	DGCR1, "DiGeorge critical region gene 1", TUP1	40103	81,83
22q11	TBX1	TBX1		40104	81,83
22q12	EWSR1	EWSR1	EWS	10750	62
				10751	VII
22q13	ARSA	ARSA	"metachromatic leucodystrophy"	40102	81,83
22q13	PDGFB	PDGFB	"becaplermin", "oncogene SIS", SSV	10742	VI
22q13	SHANK3	SHANK3	KIAA1650, "proline rich synapse associated protein 2", prosap2, PSAP2, "shank postsynaptic density protein", SPANK-2	40102	81,83
				40103	81,83
				40104	81,83
Xp11	TFE3	TFE3	bHLHe33, member A, TFEA, transcription factor E family	10741	72
				40051	77
Xp22	KAL	KAL1	"anosmin-1", KALIG-1, "WAP four-disulfide core domain 19", WFDC19	40115	90
Xp22	SHOX	SHOX	GCFX, PHOG, SHOXY, SS	40112	89
Xp22	STS	STS	ARSC, "arylsulfatase C"	40115	90
Xq12	AR	AR	AIS, HUMARA, "Kennedy disease", NR3C4, SMAX1, "testicular feminization"	10720	56
Xq13	XIST	XIST	DXS1089, LINC00001, "long intergenic non-protein coding RNA 1", NCRNA00001, swd66	40108	89

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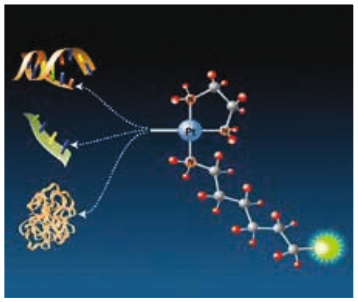

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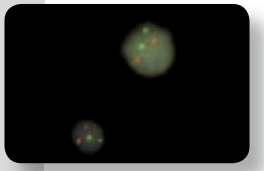
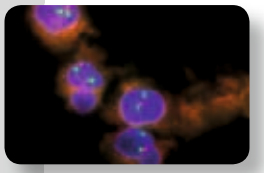
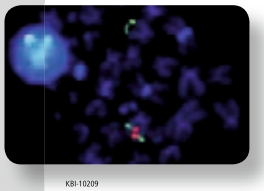


KBI-10008
t(9;22) BCR/ABL
Material kindly provided by Dr. Balogh, Budapest



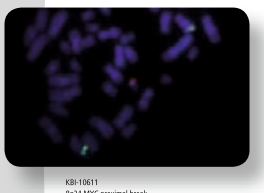
KBI-10102
13q14 DLEU deletion
Image kindly provided by Dr. Dastugue, Toulouse



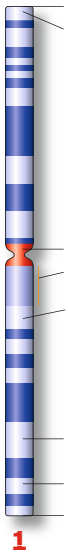
KBI-10209
5q- (5q33 deletion)
Image kindly provided by Dr. Mohr, Dresden

KBI-10306
t(6;9) DEK/NUP214
Image kindly provided by Dr. Stevens-Kroef, Nijmegen

KBI-10404
Ins(4;11) MLL/AFF1
Image kindly provided by Prof. Christine J. Harrison, Newcastle



KBI-10611
8q24 MYC proximal break
Image kindly provided by Prof. Siebert, Kiel



	Cat. # KBI-	Page
1pter	40201	92
CHD5 1p36	10507	41
	10712	60
SE1/5/19	20026	94
SE1 1qh 1q12	20001	94
	40061	77
1q21 S100A10	10503	39
CKS1B 1q21	10507	41
MDM4 1q32	10736	61
PARP1 1q42		
1qter	40202	92

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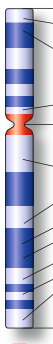

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7pter	40213	92
PMS2 7p22		
ETV1 7p21		
EGFR 7p11	10702	54
SE7 D7Z1	20007	94
	20031	14,94
	40061	77
ELN 7q11.2	40111	86
MDS 7q22	10202	25
	10207	25
MDS 7q31	40111	86
MET 7q31	10719	55
IRF5 7q32		
BRAF - KIAA1349 7q34		
MDS 7q36	10202	25
	10207	25
7qter	40214	92

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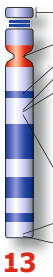

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NOR	20033	95
SE13/21	20027	94
BRCA2 13q13		
FOXO1 13q14	10716	64
RB1 13q14	40001	78
	40003	79
	40005	79
	40050	77
	40051	77
	40064	77
DLEU1 13q14	10102	17
	10113	20
	10502	38
IRS2 13q34		
13qter	40225	92

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	Cat. # KBI-	Page
19pter	40234	92
MLLT1 19p13	10307	30
ZNF443 19p13	10739	66
SE1/5/19	20026	94
PAK4 19q13.2		
PLAUR 19q13.3		
ERCC1 19q13.3	10739	66
CD37 19q13.3	10509	39
	40064	77
19qter	40235	92

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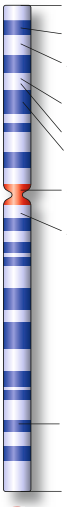

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2pter	40203	92
MYCN 2p24	10706	59
ALK 2p23	10746	54
	10747	53,73
EML4 2p21	10746	54
MSH2 2p21		
MSH6 2p16		
SE2 D2Z	20002	94
	40063	77
AFF3 2q11	10706	59
HER4 2q34		
2qter	40204	92

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	Cat. # KBI-	Page
8pter	40215	92
GATA4 8p23	40118	VII
PNOC 8p21	10503	39
FGFR1 8p11.2	10737	16,51
	12754	VI
SE8 D8Z1	20008	14,94
	20031	14,94
	40061	77
RUNX1T 8q21	10301	28
	10106	19
	10117	21
	10603	42
	10611	47
	10704	52
MYC 8q24	10749	VII
8qter	40216	92

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	Cat. # KBI-	Page
NOR	20033	95
SE14/22	20028	94
DAD1 14q11.2		
	10510	IV
	10601	22,41,44
	10602	38,47
	10603	42
	10604	43
	10605	36,47
	10606	43
	10610	37
	10729	70
BCL11b 14q32	10755	VIII
IGH 14q32	40064	77
14qter	40226	92

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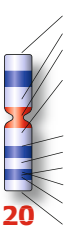

	Cat. # KBI-	Page
20pter	40236	92
20p11 Control		
SE20 D20Z1	20020	94
	40062	77
MAPRE1 20q11	10203	26
	10721	67
	10733	50
MAFB 20q12	10510	IV
PTPRT 20q12	10203	26
NCOA3 20q13.1		
NFATC2 20q13.2	10751	VII
ZNF217 20q13.2	10733	50
AURKA 20q13.2	10721	67
20qter	40237	92

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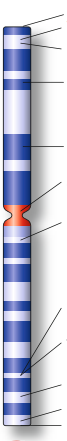

	Cat. # KBI-	Page
3pter	40205	92
VHL 3p25		
PPARγ 3p25	10707	58
MLH1 3p22		
UBA3 3p14		
SE3 D3Z1	20003	94
	40061	77
3q11 Control	10110	19
MECOM inv(3) 3q26	10204	26
	10205	27
	10310	II
TERC 3q26	10110	19
	10704	52
BCL6 3q27	10607	45
	10730	71
DLG 3q29		
3qter	40206	92

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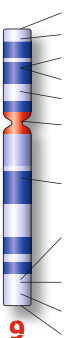

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9pter	40217	92
JAK2 9p24	10012	13
MLLT3 9p21	10308	30
CDKN2A 9p21	10402	34
PAX5 9p13	10710	52
SE9 CLASSICAL	20009	94
	40062	77
9q21	10402	34
	10710	52
miRNA 199b/ 219.2 9q34	10005	11,35
	10006	11,35
	10008	12,35
	10009	12,35
ABL1 9q34	10508	40
NUP214 9q34	10306	32
9qter	40218	92

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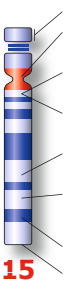

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NOR	20033	95
SE15 D15Z	20015	94
	40063	77
SNRPN 15q11	40109	85
	40116	91
UBE3A 15q11	40110	86
	40116	91
SMAD6 15q22	10504	40
	10508	40
PML 15q24	10302	29
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	40110	86
IGF1R 15q26	40116	91
15qter	40227	92

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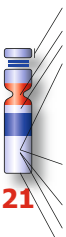

	Cat. # KBI-	Page
NOR	20033	95
SE13/21	20027	94
LIPI 21q11		
RCAN1 21q22	40002	78
	40003	79
	40005	79
	40008	79
	40050	77
	40051	77
	40064	77
RUNX1 21q22	10301	28
	10401	33
	10310	II
ERG 21q22	10726	57
TMPRSS2 21q22	10726	57
21qter	40238	92

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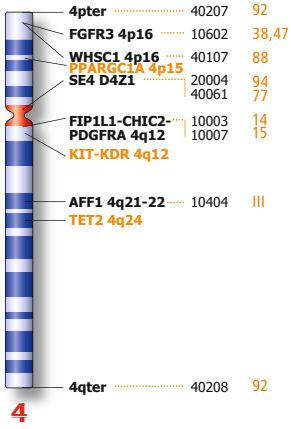

	Cat. # KBI-	Page
4pter	40207	92
FGFR3 4p16	10602	38,47
WHSC1 4p16	40107	88
PPARGC1A 4p15		
SE4 D4Z1	20004	94
	40061	77
FIP1L1-CHIC2-	10003	14
PDGFRA 4q12	10007	15
KIT-KDR 4q12		
AFF1 4q21-22	10404	III
TET2 4q24		
4qter	40208	92

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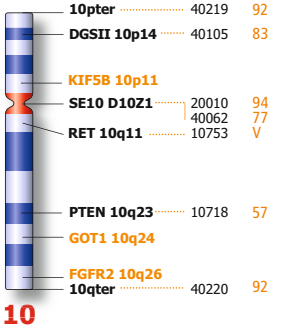

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10pter	40219	92
DGSII 10p14	40105	83
KIF5B 10p11		
SE10 D10Z1	20010	94
	40062	77
RET 10q11	10753	V
PTEN 10q23	10718	57
GOT1 10q24		
FGFR2 10q26		
10qter	40220	92

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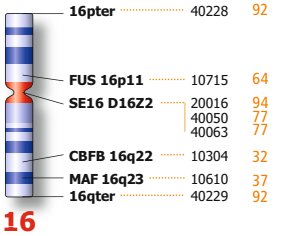

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16pter	40228	92
FUS 16p11	10715	64
SE16 D16Z2	20016	94
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	40063	77
CBFB 16q22	10304	32
MAF 16q23	10610	37
16qter	40229	92

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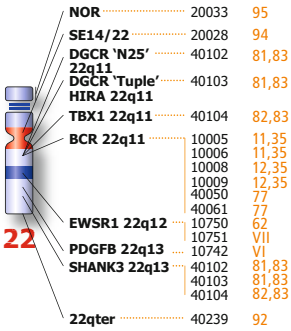

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NOR	20033	95
SE14/22	20028	94
DGCR 'N25'	40102	81,83
22q11		
DGCR 'Tuple'	40103	81,83
HIRA 22q11		
TBX1 22q11	40104	82,83
BCR 22q11	10005	11,35
	10006	11,35
	10008	12,35
	10009	12,35
	40050	77
	40061	77
EWSR1 22q12	10750	62
	10751	VII
PDGFB 22q13	10742	VI
SHANK3 22q13	40102	81,83
	40103	81,83
	40104	82,83
22qter	40239	92

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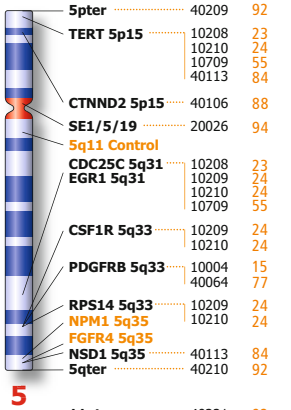

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5pter	40209	92
TERT 5p15	10208	23
	10210	24
	10709	55
	40113	84
CTNND2 5p15	40106	88
SE1/5/19	20026	94
5q11 Control		
CDC25C 5q31	10208	23
EGR1 5q31	10209	24
	10210	24
	10709	55
CSF1R 5q33	10209	24
	10210	24
PDGFRB 5q33	10004	15
	40064	77
RPS14 5q33	10209	24
NPM1 5q35	10210	24
FGFR4 5q35		
NSD1 5q35	40113	84
5qter	40210	92

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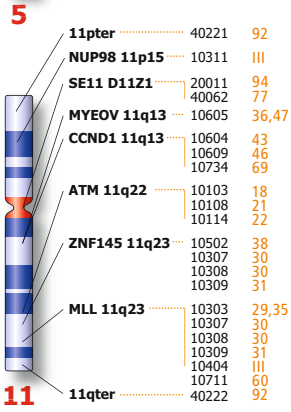

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11pter	40221	92
NUP98 11p15	10311	III
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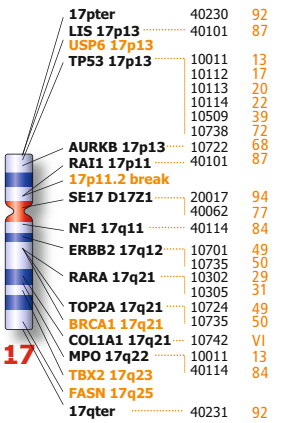

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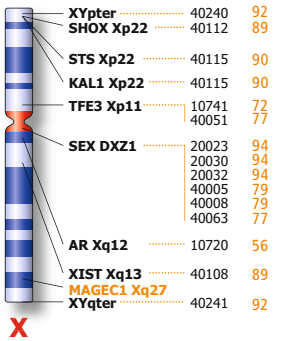

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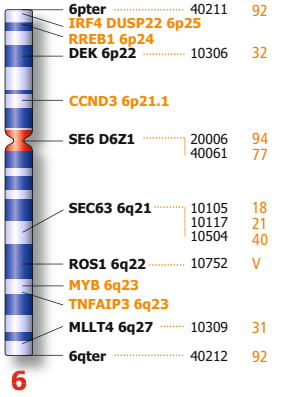

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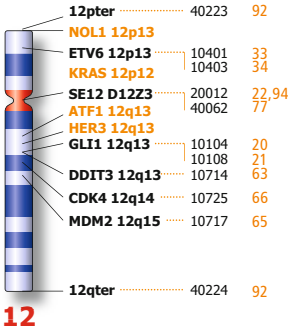

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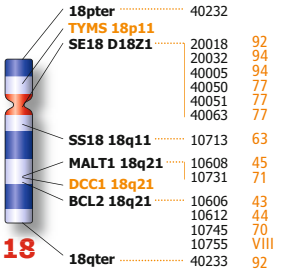

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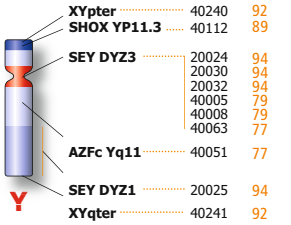

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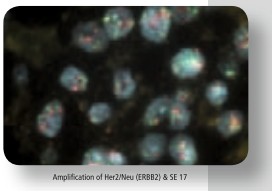
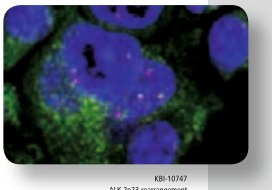
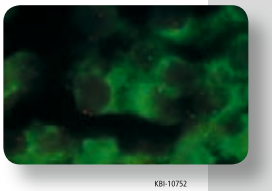


Amplification of Her2/Neu (ERBB2) & SE 17



KBI-10747
ALK 2p23 rearrangement
Image kindly provided by Prof. B. Terris, Dr. P.A. Just, Paris



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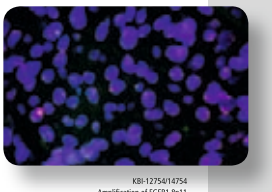

KBI-12754/14754
Amplification of FGFR1 8p11
Image kindly provided by Dr. Marcus Otte, ORIDIS Biomarkers, Vienna

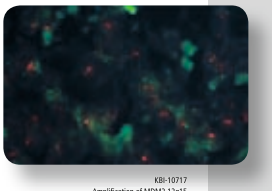

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Image kindly provided by W. Griffioen, Arnhem

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KREATECH DIAGNOSTICS

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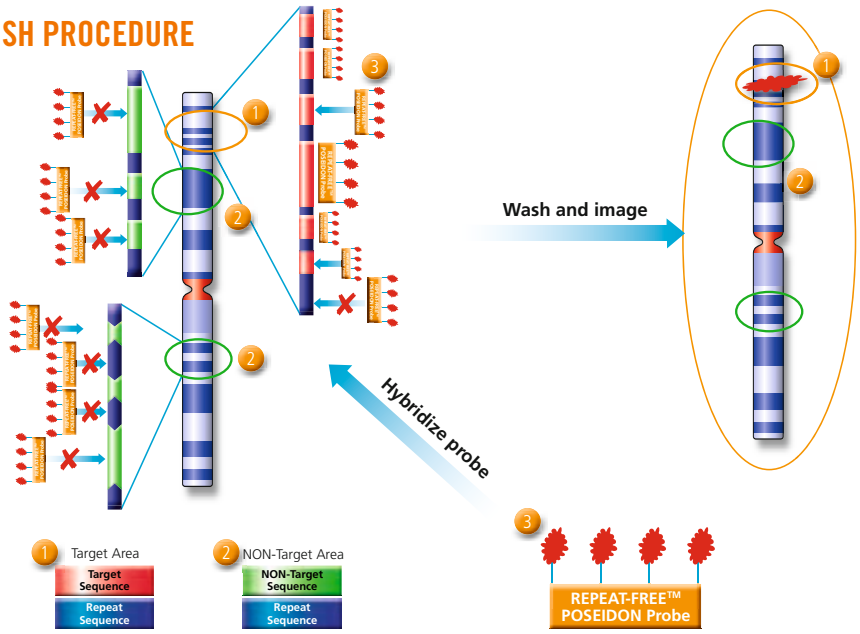
REPEAT-FREE™ POSEIDON™ FISH PROCEDURE



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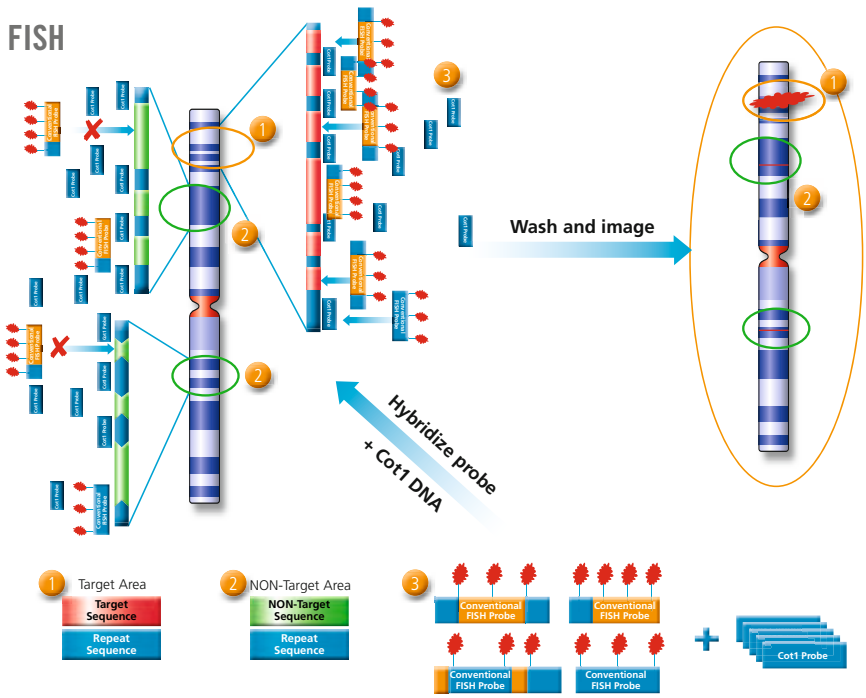
CONVENTIONAL FISH PROCEDURE



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