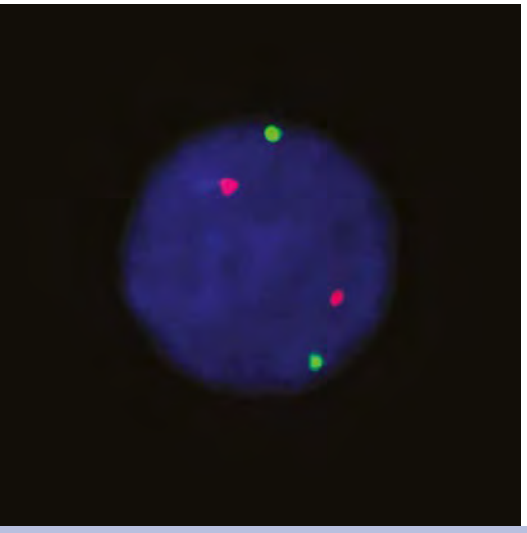
Oxford Gene Technology

The Molecular Genetics Company™

Cytocell
an OGT company

SureSeq™



CytoSure™

Product Catalogue

2017-2018

- Cytocell® FISH probes
- SureSeq™ NGS products
- CytoSure™ Array products

Oxford Gene Technology (OGT) offers high-quality integrated technologies to detect a complete range of genetic aberrations. Our products are backed by deep technical expertise and dedicated customer support. Custom product capabilities – including myProbes® custom FISH probes, myPanel™ custom NGS panels and custom arrays – are also available.

Cytocell
an OGT company

FISH probes

SureSeq™

NGS products

CytoSure™

Array products

An Introduction

Oxford Gene Technology — The Molecular Genetics Company™

Reflecting our commitment to the field of molecular genetics and our position as a leading solution provider to the global genomics market, this 2017-2018 catalogue marks the first time we have included our complete portfolio of genomics products in one reference. Our integrated portfolio provides our customers with the most advanced tools available to detect a comprehensive range of genetic variations in cancer, cytogenetics, rare disease and reproductive health.

Recent years have seen significant growth for Oxford Gene Technology (OGT), including the addition of Cytocell® FISH probes to our portfolio in 2014. For over 25 years, Cytocell probes have been regarded as the gold-standard for fluorescence *in situ* hybridisation (FISH), offering the largest collection of high-quality FISH probes available from one supplier. In addition, our myProbes® service further utilises our experience and expertise, allowing the creation of custom built probes tailored to a researcher's exact needs and specifications.

Combined with our technologies in NGS and arrays, OGT is able to provide comprehensive high-value solutions for detecting the causative variations underlying genetic disease.

Our integrated portfolio comprises:

- **Cytocell FISH probes** — Fluorescence *in situ* hybridisation (FISH) probes for detecting gene rearrangements related to inherited genetic disease and cancer
- **SureSeq™ NGS products** — An expanding portfolio of next generation sequencing (NGS) panels and library preparation products for the accurate detection of genetic variants
- **CytoSure™ array products** — A broad range of array products for cytogenetics, rare disease, cancer and reproductive health research

OGT is proud to support the important work our customers are doing around the world and we are committed to delivering the highest quality products and customer service. If you would like more detailed information on our extensive product range, please visit www.ogt.com and www.cytocell.com.

Dr. Mike Evans
CEO, Oxford Gene Technology

Disclaimer

CytoSure™, SureSeq™ and myProbes®: For Research Use Only; Not for Use in Diagnostic Procedures. Cytocell: Some products may not be available in the US.

Contents

Haematology

Multiprobe Haematology

Haematopathology

Pathology

Pathology continued

Prenatal

Microdeletion

Paints

Satellites

Subtelomere Specific Probes

ZooFISH

Custom FISH Probes

FISH Accessories

Next Generation Sequencing (NGS)

Array Products

Indices of FISH probes

Cytocell FISH products

OGT's product portfolio includes Cytocell DNA diagnostic fluorescence *in situ* hybridisation (FISH) kits aimed at two disciplines: constitutional cytogenetics and haematology/pathology cytogenetics.

We offer three key product ranges:

Chromoprobe Multiprobe® Macroarray Range

Using our unique Chromoprobe® process, multiple probes are reversibly bound to a glass slide providing a convenient screening tool for genetic abnormalities across multiple chromosomes. Key applications include detection of chromosomal rearrangements and as a diagnostic / prognostic tool in the detection of various leukaemias.

Aquarius® Range

Aquarius® probes are directly labelled liquid probes provided in hybridisation solution. The probes are accompanied by DAPI counterstain to provide a complete fluorescence *in situ* hybridisation kit.

myProbes®

myProbes® is a custom FISH probe design and manufacture service, which utilises Cytocell's proprietary BAC clone collection. If a product you require does not appear in the catalogue, do not hesitate to contact Cytocell with your request.

Patents and Trademarks

Aquarius, Chromoprobe, Cytocell, Chromoprobe Multiprobe and myProbes are registered trademarks of Cytocell Ltd.

The Chromoprobe principle is covered by international patents WO9314223, EP0623177. The design of the Multiprobe is a registered design and is also covered by a Design Patent No. 420,745.

Cytocell is registered with the MHRA (Medicines and Healthcare products Regulatory Agency) and all Cytocell products are CE marked in accordance with the *In-Vitro* Diagnostic Medical Devices Directive 98/79/EC, and the 2002 Regulations. Cytocell operates a quality management system that have been assessed and certified to both EN ISO 9001:2008 and EN ISO 13485:2003.

Aquarius® FISH probes contain technology licensed from Life Technologies Corporation that is available for human diagnostics or life science research use only.

Please check our website for the latest probe ranges available from Cytocell. www.cytocell.com

990213_CAT_Cytocell_v001/2016_08_ROW

Cytocell FISH probes are developed and produced in the UK

Aquarius® Overview

The Aquarius® range consists of directly labelled FISH probes for constitutional cytogenetic and oncology applications.

All Aquarius® probes provide the benefits of:

- Economical kit formats: 5 and 10 tests. Prenatal probes are also available in 30 or 50 test formats.
- Stable liquid reagents premixed in hybridisation solution, provided with DAPI counterstain and full instructions for use.
- Directly labelled probes allowing visualisation with standard (FITC, Texas Red®, aqua and DAPI) microscope filters.
- Designed for FISH on interphase nuclei and metaphase chromosomes.

The procedure is simple:

1. 

   Spot slide with cell sample and dehydrate through an ethanol series.

2. 

   Apply Aquarius® probe onto dehydrated cell sample.

3. 

   Place coverslip onto slide and seal.

4. 

   Denature on a hotplate and hybridise according to the information for users (IFU) pack insert.

5. 

   Wash with rapid, formamide-free stringency washes.

6. 

   Apply DAPI counterstain provided and view under a fluorescent microscope.

Multiprobe Overview

Cytocell an OGT company multiprobe

The Chromoprobe Multiprobe® System is an extension of Cytocell's proprietary Chromoprobe® technology, whereby DNA FISH probes are reversibly bound to the surface of a glass device. These probes dissolve back into solution once in contact with the supplied hybridisation buffer, whilst denaturation of the probes and target DNA occurs simultaneously under the device once heated. This approach not only simplifies the whole FISH procedure but also renders it safer and quicker to use.

This system allows multiple FISH probes to be hybridised on the same slide in a spatially separated manner allowing rapid screening of a patient sample for a number of different DNA sequences in a single FISH analysis.

The assay is supplied in a kit format of 2, 5 or 10 devices and includes hybridisation solution, DAPI counterstain, template slides, a hybridisation chamber and full instructions for use. The kit even contains a unique liquid crystal display slide surface thermometer for accurate temperature measurement of the denaturation surface.

The procedure is simple:

1

Soak the slides in 100% methanol, then polish dry with a lint free cloth.

2

Spot 4µl (or 2µl for a 24 square device) of cell sample onto alternate squares of the supplied slide.

3

Once dry, fill in the remaining squares with the cell sample and check using phase contrast.

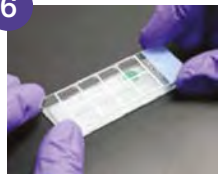
4

Place slides in 2xSSC for 2 minutes and then dehydrate through an ethanol series.

5

Spot 2µl (or 1µl for a 24 square device) of supplied hybridisation solution onto each square of the device.

6



Carefully lower spotted slide onto the device.

7

Check the temperature of the hotplate using the slide surface thermometer provided. Denature the slide/device at 75°C for 2 minutes (or 5 minutes for OctoChrome™ device).

8

Place slide/device in hybridisation chamber supplied and float on the surface of a clean 37°C waterbath overnight.

9

Wash in 0.4xSSC at 72°C for 2 minutes, then 2xSSC/0.05% Tween at room temperature for 30 seconds.

10

Apply DAPI counterstain provided and view under a fluorescence microscope.

Tissue Pretreatment Overview

Introducing a pretreatment kit capable of preparing slides for CISH and/or FISH analysis on formalin-fixed, paraffin-embedded (FFPE) tissue.

Our ready-to-use Tissue Pretreatment Kit has been optimised to produce excellent visual results with our extensive Aquarius® Pathology FISH range.

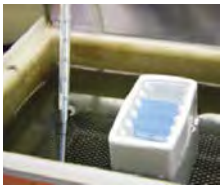
To further extend the utility of the kit we have also validated its use with other commercially available CISH (chromogenic *in situ* hybridisation) and FISH (fluorescence *in situ* hybridisation) DNA probes.

With ease-of-use and convenience in mind, our simple two stage FFPE slide preparation protocol employs the use of ready-to-use reagents that have been optimised to increase the permeabilisation of cell membranes and facilitate penetration of the desired FISH or CISH DNA probe.

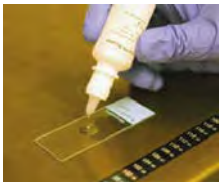
The procedure is simple:

1. 

   Deparaffinise slides and rehydrate through an ethanol series.

2. 

   Place slides into Tissue Pretreatment Solution (Reagent 1), preheated to 100°C.

3. 

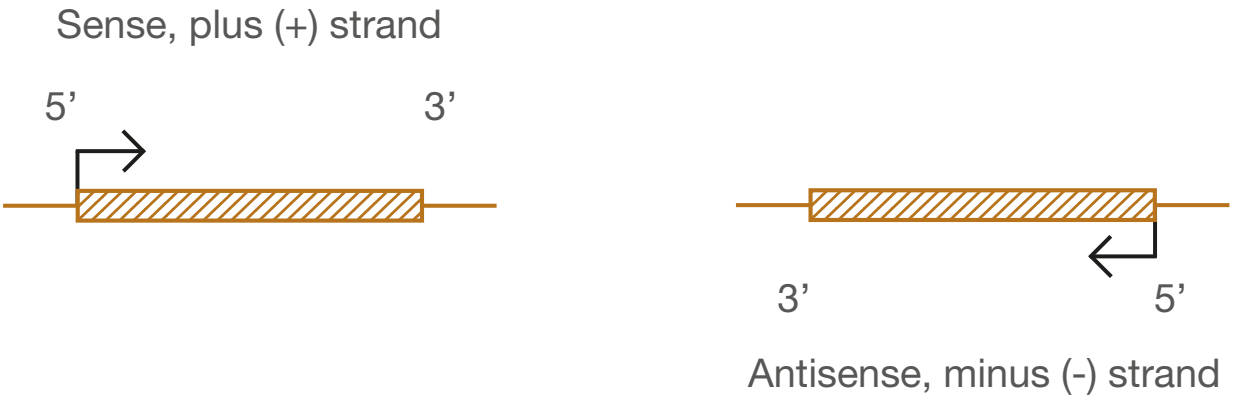
   Rinse slides and apply Enzyme Reagent provided.

4. 

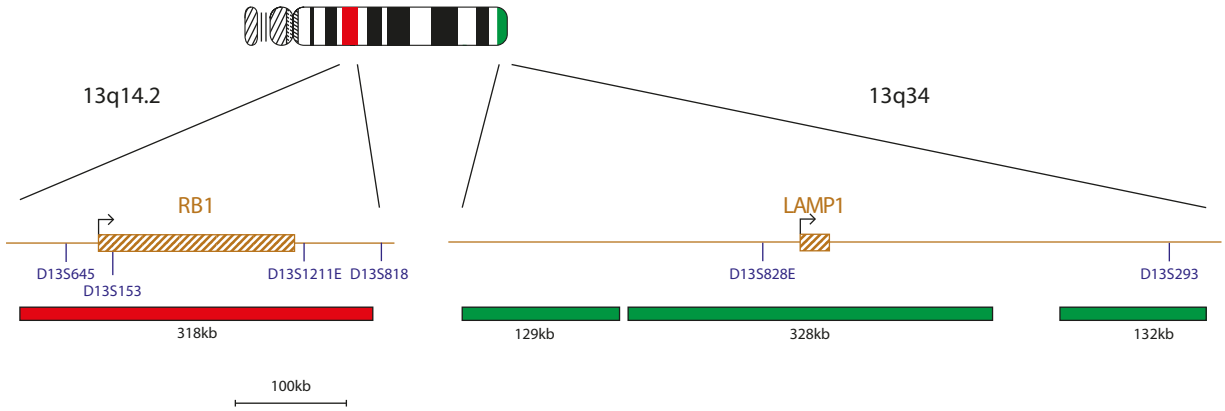
   Dehydrate slides through an ethanol series and continue with FISH denaturation and hybridisation protocol.

Probe Maps

Probe maps in this 2017-2018 version of the Cytocell catalogue have been updated to include information on gene orientation to allow the 3' or 5' positions of the probes to be seen in relation to the gene, or region, of interest. The arrows on the genes indicate the direction of transcription. Those with an arrow above, pointing to the right, are located on the plus, or sense, strand of the DNA. Those with an arrow below the gene, pointing to the left, are on the minus, antisense strand. In both cases, the 5' end is that with the arrow, as genes are transcribed in a 5' to 3' direction. Examples can be seen below.



Example of a typical Cytocell product map.



HGNC Nomenclature

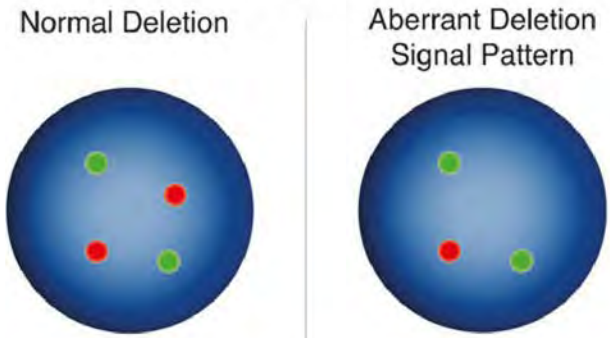
Gene names have also been updated to reflect current HUGO Gene Nomenclature Committee (HGNC) approved symbols. Where this affects existing product names, the approved HGNC symbol is placed into brackets. All gene names were checked and updated according to the HGNC database[1] as of January 2016.

REFERENCES

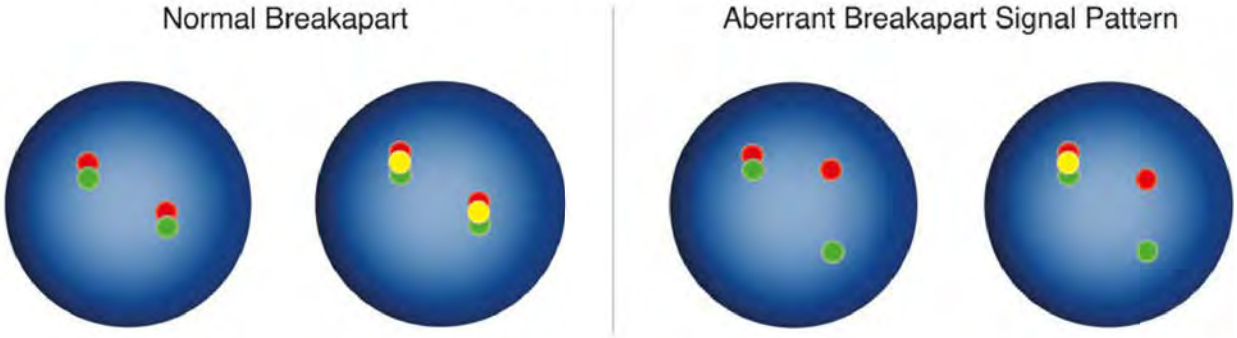
1. HGNC Database, HUGO Gene Nomenclature Committee (HGNC), EMBL Outstation - Hinxton, European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, Cambridgeshire, CB10 1SD, UK. www.genenames.org

Common FISH

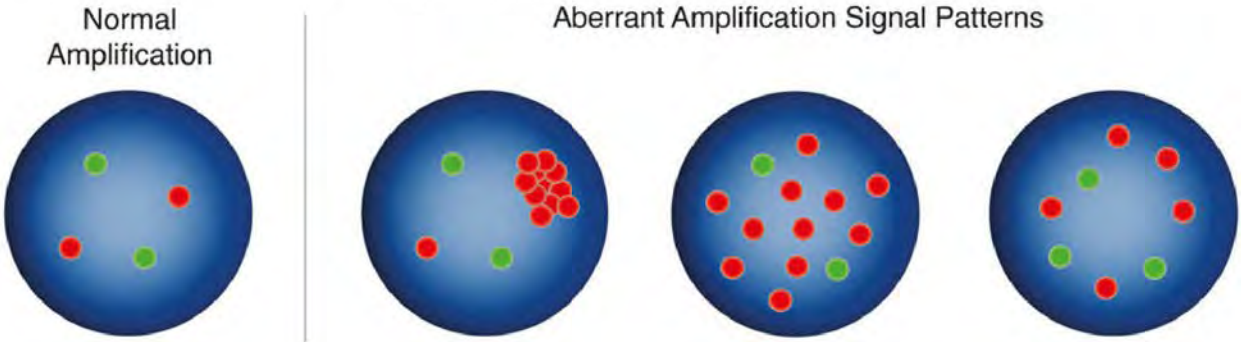
Deletion Signal Patterns



Breakapart Signal Patterns



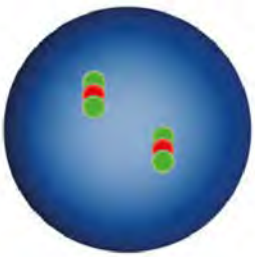
Amplification Signal Patterns



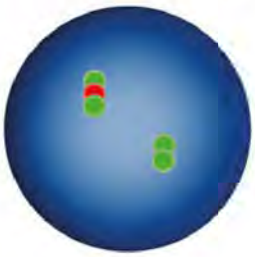
Signal Patterns

Deletion Fusion Signal Patterns

Normal Deletion Fusion

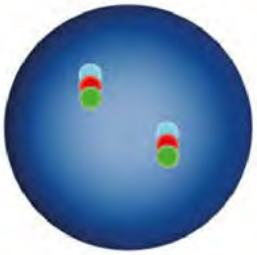


Aberrant Deletion Fusion Signal Pattern

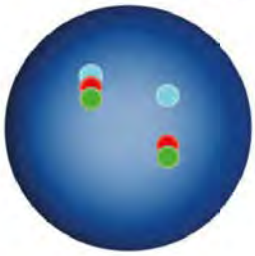


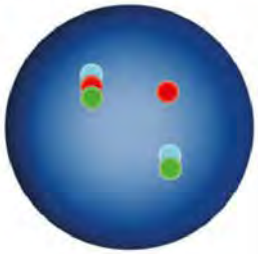
3 Colour Breakapart Signal Patterns

Normal 3 Colour Breakapart



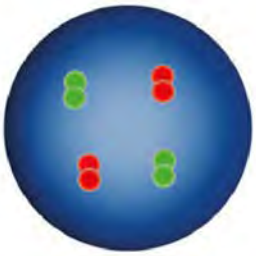
Aberrant 3 Colour Breakapart Signal Patterns



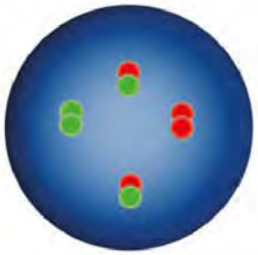


Translocation Dual Fusion Signal Patterns

Normal Translocation Dual Fusion



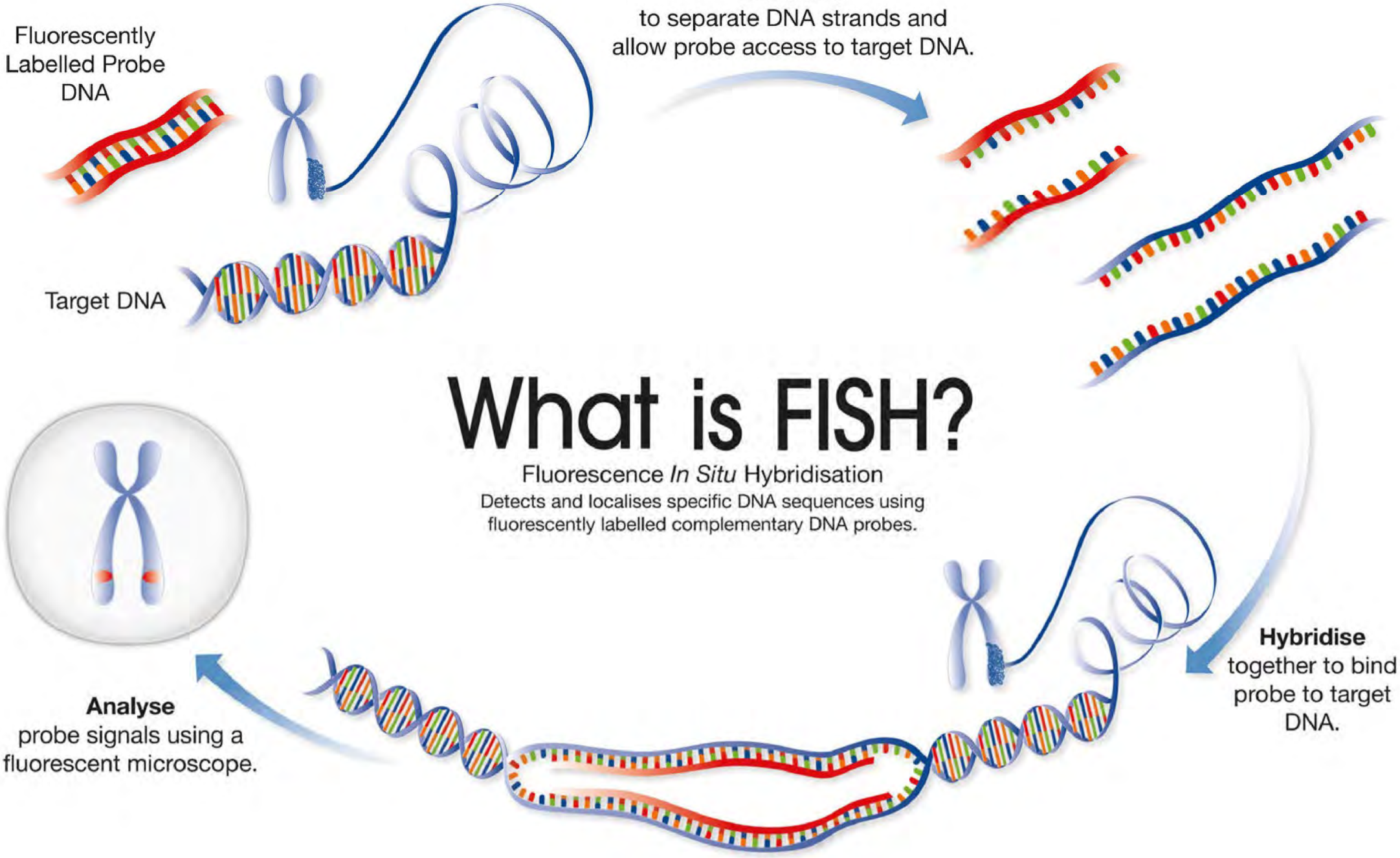
Aberrant Translocation Dual Fusion Signal Pattern



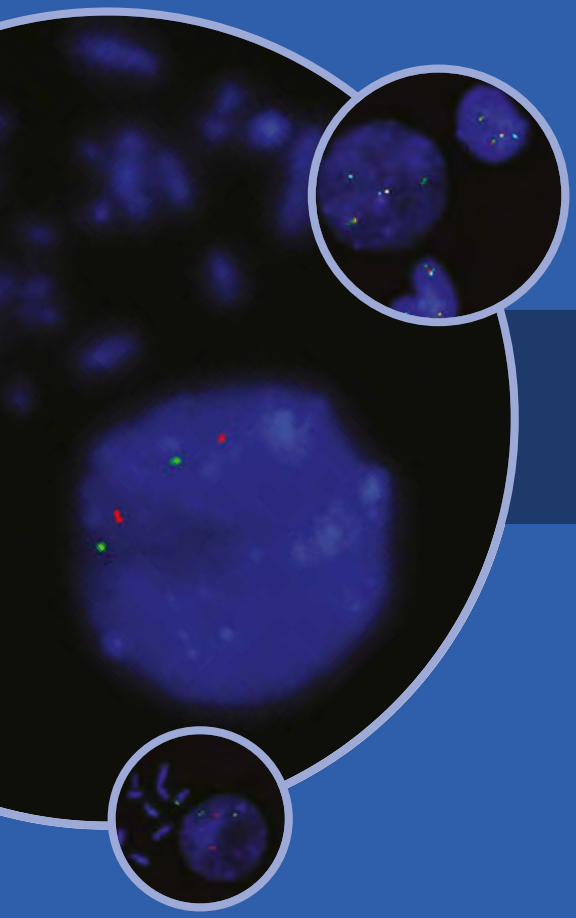
What is FISH?

Fluorescence *In Situ* Hybridisation

Detects and localises specific DNA sequences using fluorescently labelled complementary DNA probes.



Cytocell
an OGT company
aquarius



Haematology

Contents

Refer to our Haematology key to determine the most commonly associated disease state for each of our Haematology products, as supported by literature.

Haematology key: **

- ALL — Acute Lymphoblastic Leukaemia
- AML — Acute Myeloid Leukaemia
- CLL — Chronic Lymphocytic Leukaemia
- CML — Chronic Myeloid Leukaemia
- L — Lymphoma
- MM — Multiple Myeloma
- MDS — Myelodysplastic Syndrome
- MPN — Myeloproliferative Neoplasm

** These roundels are only to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Haematology

As long ago as the 19th century, nuclear changes were recognised as being significant in cancer biology. Advances in cytogenetics and molecular cytogenetics in the last century showed that although a number of numerical and structural chromosome changes appeared to be random and non-specific, rearrangements involving individual chromosomes were shown to define specific abnormalities in individual tumour types.

Fluorescence *in situ* hybridisation (FISH), using locus-specific probes that are capable of defining these stereotypic structural rearrangements, has now become a routine diagnostic test in the clinical laboratory and the technique has thus been shown to be useful in the management of cancer patients.

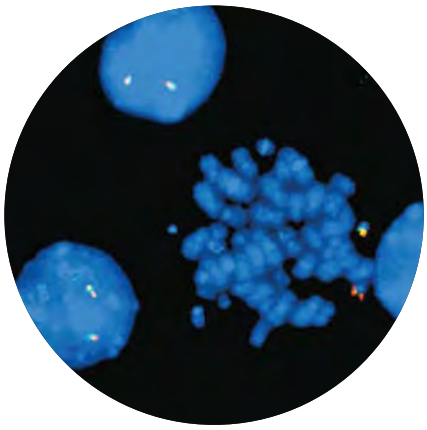
Cytocell offers a range of FISH probes, specific for a number of haematological malignancies, which are available in the Aquarius® liquid format. These probes are directly labelled, ready to use in hybridisation buffer and available in economical five, and larger ten, test kits. The protocol is rapid and simple and has been developed to allow co-denaturation of the FISH probe and target DNA simultaneously.

The probe mixtures are designed for use on interphase nuclei and metaphase chromosomes from cultured peripheral blood cells or cultured bone marrow samples.

Cytocell an OGT company aquarius

Cat. No. **LPH 027-S** (5 tests)
Cat. No. **LPH 027** (10 tests)

AML1 (RUNX1) Breakapart



AML ALL **

The RUNX1 (*runt related transcription factor 1*) gene at 21q22.12 is one of the most frequent targets of chromosomal rearrangements observed in human acute leukaemia.

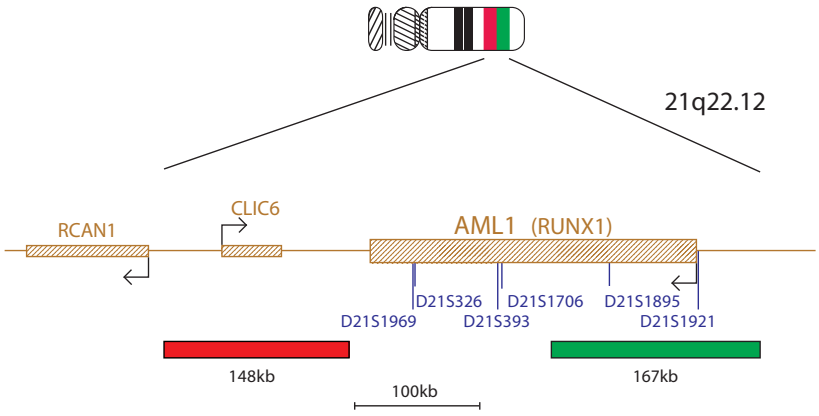
The most common rearrangements are the ETV6-RUNX1 and RUNX1-RUNX1T1 fusions. The ETV6-RUNX1 fusion is brought about by the t(12;21)(p13;q22) translocation, observed in around 21% of childhood B-cell acute lymphoblastic leukaemia (ALL) cases[1], whilst the RUNX1-RUNX1T1 fusion is the result of the t(8;21)(q22;q22) translocation observed in 10-22% of patients with acute myeloid leukaemia (AML) FAB (French-American-British classification) type M2 and 5-10% of AML cases overall[2,3]. Both these rearrangements are considered good prognostic indicators in these diseases[4,5].

The RUNX1 gene is also rearranged in many other rarer translocations, with partners including chromosomes 1, 2, 3, 4, 5, 6, 7, 9, 10, 14, 15, 16, 17, 18, 19, 20 and X[6]. This breakapart probe has been designed to allow the detection of rearrangements regardless of the partner gene.

Rearrangements of RUNX1 are not restricted to translocations. Using FISH, amplifications of chromosome 21 (iAMP21), including the RUNX1 gene, have also been found in childhood ALL[7,8]. These amplifications have been associated with poorer outcome[9].

REFERENCES

1. Jamil A *et al*., Cancer Genet Cytogenet 2000;122(2):73-8
2. Swerdlow *et al*., editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissue, Lyon, France, IARC,2008
3. Reikvam H, *et al*. J Biomed Biotechnol. 2011; 2011:104631.
4. Shurtleff *et al*., Leukemia. 1995 Dec;9(12):1985-9
5. Cho *et al*., Korean J Intern Med. 2003 Mar;18(1):13-20
6. De Braekeleer et al., Anticancer Research 2009;29(4):1031-1038
7. Niini T, Haematologica 2000;85(4):362-6
8. Harewood *et al*., Leukemia. 2003 Mar;17(3):547-53
9. Robinson HM *et al*., Leukemia 2003;17(11):2249-50

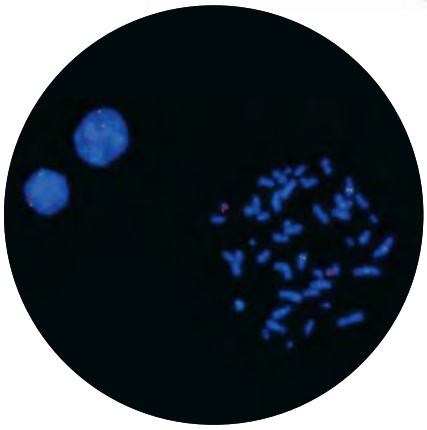


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 026-S** (5 tests)
Cat. No. **LPH 026** (10 tests)

AML1/ETO (RUNX1/RUNX1T1) Translocation, Dual Fusion

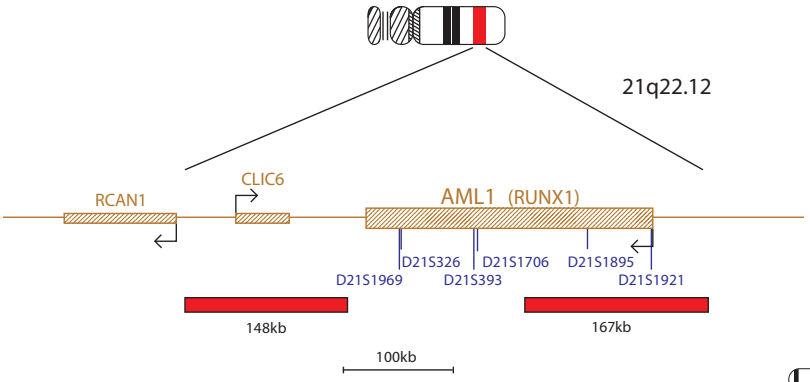


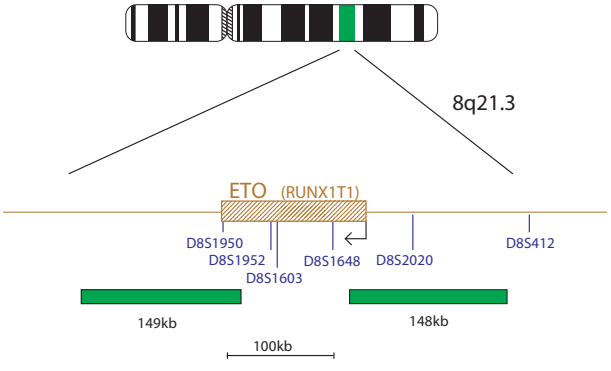
AML **

The RUNX1 (*runt related transcription factor 1*) gene at 21q22.12 is fused with the RUNX1T1 (*runt related transcription factor 1; translocated to, 1 [cyclin D related]*) gene at Ensembl location 8q21.3, in the t(8;21)(q22;q22) translocation, found most commonly in patients with acute myeloid leukaemia (AML) FAB (French-American-British classification) type M2.

AML with a RUNX1-RUNX1T1 fusion resulting from a t(8;21)(q22;q22) translocation is a recognised disease entity according to the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia[1]. The translocation is observed in 10-22% of patients with AML FAB type M2 and 5-10% of AML cases overall, most commonly in children and young adults[2] and is a good prognostic indicator[3,4,5]. The t(8;21) breakpoint mainly occurs in the intron between exons 5 and 6, just before the transactivation domain and the fusion protein created contains the DNA-binding domain of RUNX1 fused to the transcription factor RUNX1T1[2].

In addition to the reciprocal t(8;21) translocation creating the RUNX1-RUNX1T1 fusion, variant translocations have also been reported. These variant rearrangements may be cryptic and easily overlooked by G-banding; however, FISH can indicate the presence of such rearrangements[2].





REFERENCES

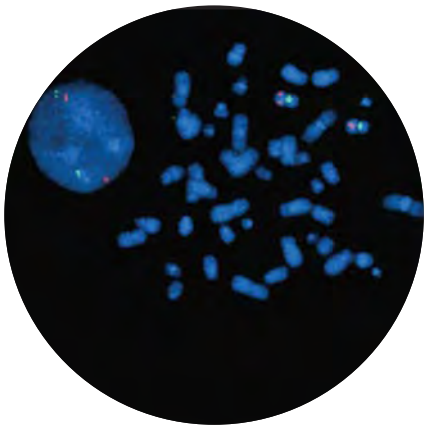
1. Swerdlow *et al*., editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissue, Lyon, France, IARC,2008
2. Reikvam H, *et al*. J Biomed Biotechnol. 2011; 2011:104631
3. Grimwade *et al*., Blood 2001;98(5):1312-1320
4. Harrison *et al*., Journal of Clinical Oncology 2010;28(16):2674-2681
5. Grimwade *et al*., Blood 2010;116(3):354-365

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 011-S** (5 tests)
Cat. No. **LPH 011** (10 tests)

ATM Deletion

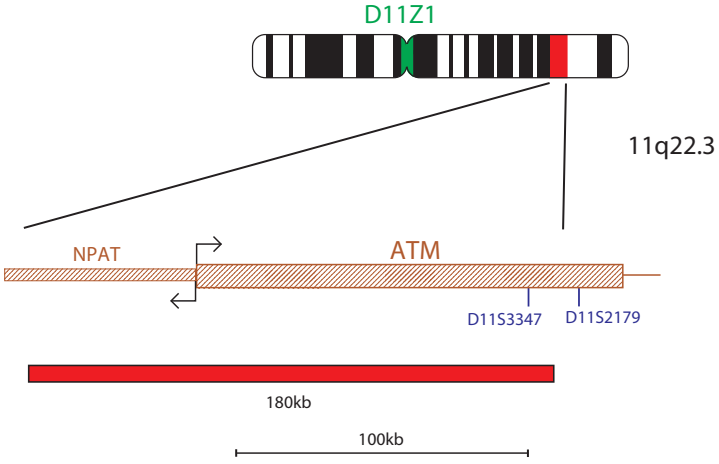


CLL **

The protein kinase ATM (*ATM serine/threonine kinase*) gene at 11q22.3, is frequently deleted in cases of B-cell chronic lymphocytic leukaemia (CLL). ATM is an important checkpoint gene involved in the management of cell damage. Its function is to assess the level of DNA damage in the cell and attempt repair by phosphorylating key substrates involved in the DNA damage response pathway[1].

B-CLL is the most common leukaemia in adults; its course can vary from very indolent to rapidly progressive. Due to the low mitotic activity of the leukaemic cells *in vitro*, clonal chromosomal abnormalities are detected in 40-50%[2] of cases by conventional cytogenetics using B-cell mitogens, whereas FISH analysis identifies chromosomal aberrations in approximately 80%[2] of B-CLLs. Screening for deletions of ATM and/or TP53 is vital to allow informed therapy choices for B-CLL patients, as deletions of TP53 and ATM confer poorer prognosis in this disease[4]; therefore, the use of FISH has proved to be a powerful tool in both the diagnosis and management of patients with B-CLL[2,3,4].

Analysis of the ATM/TP53 interaction in B-CLL has shown that TP53 and ATM play an important role in the proliferation of lymphoid cancer[1]. It has been shown that ATM enhances the phosphorylation of TP53, should the damage be so great that the cell requires destruction by apoptosis (which is mediated by TP53). Deletion of ATM removes this checkpoint activity and hence activation of TP53. Thus, there is no attempt made to repair, or apoptosis of, damaged cells, despite the presence of TP53. In the absence of ATM, damaged cells are allowed to continue to proliferate[5].



REFERENCES

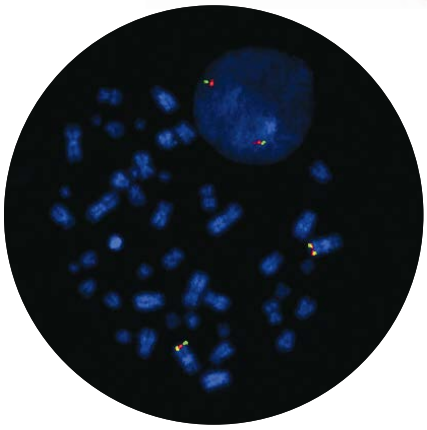
1. Stankovic *et al*., Blood 2004;103(1):291-300
2. Dohner *et al*., N Eng J Med 2000;343:1910-1916
3. Zent *et al*., Blood 2010;115(21):4154-4155
4. Rossi *et al*., Blood 2013;121(8):1403-1412
5. Khanna *et al*., Nature Genetics 1998;20(4):398-400

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 035-S** (5 tests)
Cat. No. **LPH 035** (10 tests)

BCL6 Breakapart*



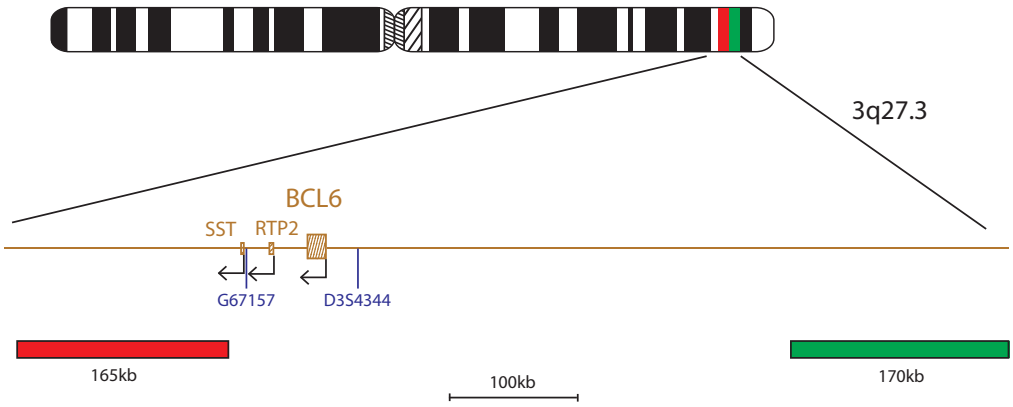
L **

Chromosomal rearrangements involving the BCL6 (*B-cell CLL/lymphoma 6*) gene at 3q27 are recognised recurrent abnormalities commonly seen in patients with B-cell malignancy[1].

BCL6 rearrangements are the most common chromosomal abnormalities seen in diffuse large B-cell lymphoma (DLBCL), occurring in up to 35% of cases[2]. They are also seen frequently in follicular lymphoma, where they occur in up to 15% of cases[3]. BCL6 is expressed in normal germinal centre B-cells and follicle helper T-cells. BCL6 translocations alter expression by promoter substitution and cause deregulated expression of normal BCL6 protein[1,4].

Approximately 50% of BCL6 translocations will involve one of the three immunoglobulin loci (IGH, IGL or IGK); the remainder of translocations involve one of more than twenty different non-immunoglobulin genes[5]. Additionally, gains and amplifications of the BCL6 gene have also been reported in cases of B-cell lymphoma[6].

The presence of concurrent BCL6 rearrangements with MYC and/or BCL2 rearrangements in patients with 'dual-hit' lymphoma has been shown to be associated with aggressive disease[7].



REFERENCES

1. Wagner SD, *et al*. Br J Haematol. 2011 Jan;152(1):3-12
2. Lossos I, *et al*. Leukemia. 2003; 17(7): 1390-7
3. Akasaka T, *et al*.. Blood. 2003;102(4):1443-8
4. Ye BH, *et al*. EMBO J 1995 Dec 15;14(24):6209-17
5. Ohno H. J Clin Exp Hematop 2006 Nov;46(2):43-53
6. Karube K, *et al*. Mod Pathol 2008;21(8):973-8
7. Aukema SM, *et al*. Blood. 2011; Feb 24;117(8):2319-31

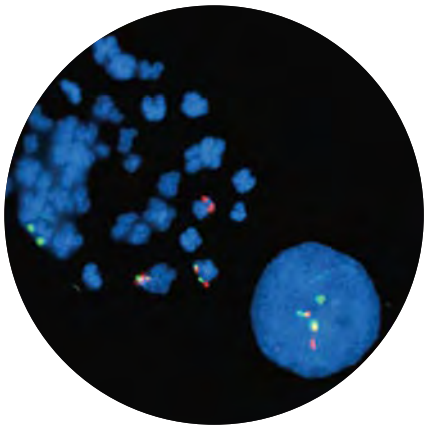
*** A similar product is also available within the Haematopathology range, refer to page 84.**

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 007-S** (5 tests)
Cat. No. **LPH 007** (10 tests)

BCR/ABL (ABL1) Translocation, Dual Fusion



BCR-ABL (ABL1) positive sample

ALL AML CML **

The BCR (*breakpoint cluster region*) gene is located at 22q11.23 and the ABL1 (*ABL proto-oncogene 1, non-receptor tyrosine kinase*) gene is located at 9q34.12. Translocation between these two genes gives rise to the BCR-ABL1 fusion gene, and produces a Philadelphia chromosome; the visible result of this translocation.

The presence of a BCR-ABL1 fusion has important diagnostic and prognostic implications in a number of haematological disorders.

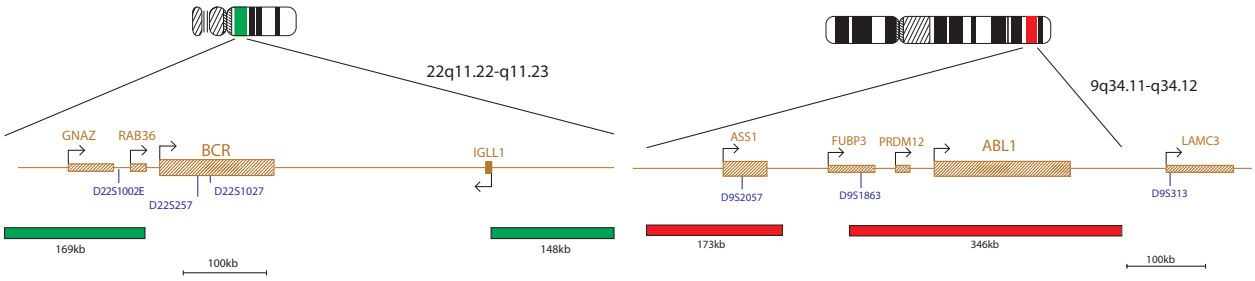
The t(9;22)(q34.12;q11.23) translocation is the hallmark of chronic myeloid leukaemia (CML) and is found in around 90-95% of cases[1]. The remaining cases have a variant translocation, or have a cryptic rearrangement involving 9q34 and 22q11.23 that cannot be identified by routine cytogenetic analysis[1].

The BCR-ABL1 fusion can also be found in 25% of adult acute lymphoblastic leukaemia (ALL) and in 2-4% of childhood ALL[1]. The presence of a BCR-ABL1 fusion has been shown to confer a poor prognosis in ALL in both adults and children[1,2]. The detection of the abnormality is therefore of high importance for risk stratification, which will influence treatment and management decisions[2]. In a small number of ALL cases, the translocation does not result in a cytogenetically visible Philadelphia chromosome. In these cases, FISH is essential for highlighting the fusion gene[3].

This rearrangement is also seen in rare cases of acute myeloid leukaemia (AML). Philadelphia-positive AML is characterized by its resistance to conventional standard chemotherapy and poor prognosis[4], so accurate and rapid identification of this chromosomal abnormality is vital.

REFERENCES

1. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France, IARC:2008
2. Harrison *et al*., BJH 2010;151:132-142
3. Van Rhee *et al*., Br j Haematol 1995;90:225-8
4. Soupir *et al*., Am J Clin Pathol 2007;127:642-650

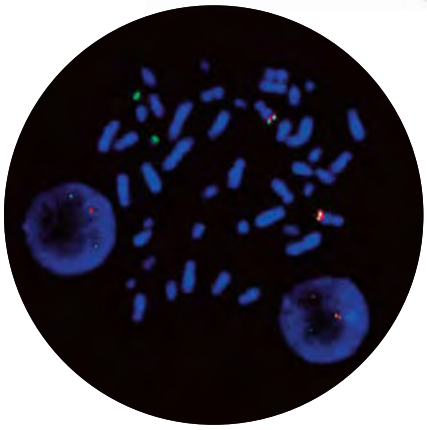


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 038-S** (5 tests)
Cat. No. **LPH 038** (10 tests)

BCR/ABL (ABL1) *Plus* Translocation, Dual Fusion



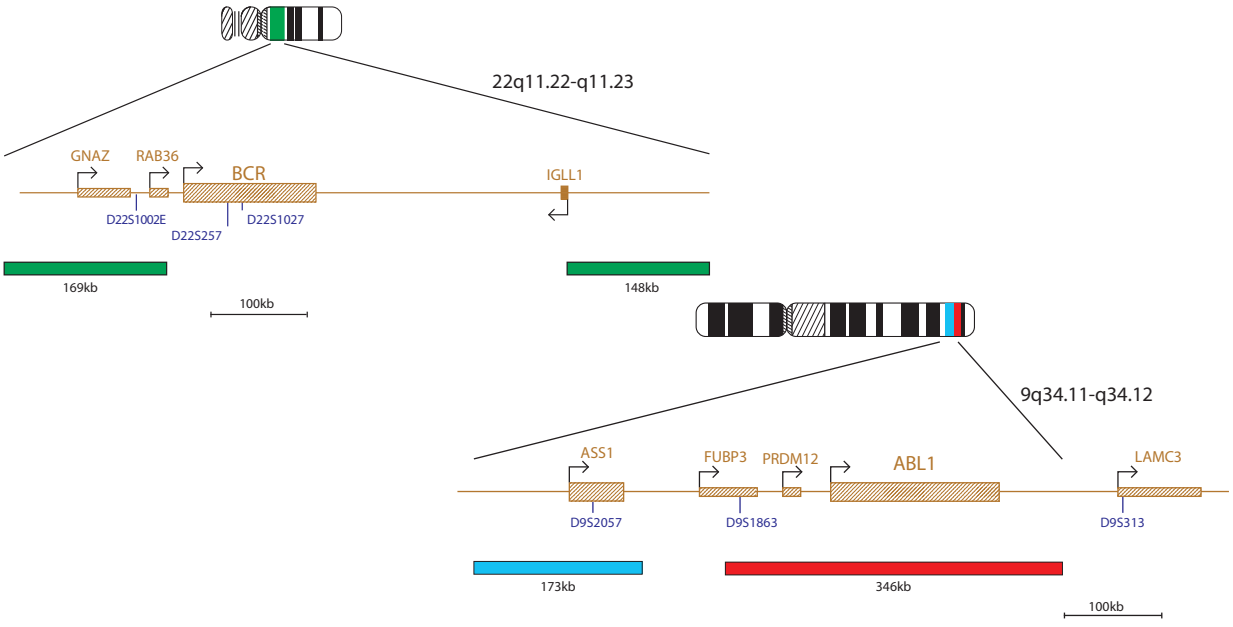
ALL AML CML **

The BCR (*breakpoint cluster region*) gene is located at 22q11.23, the ABL1 (*ABL proto-oncogene 1, non-receptor tyrosine kinase*) gene is located at 9q34.12 and the ASS1 (argininosuccinate synthase 1) gene is located at 9q34.11. Translocation between BCR and ABL1 gives rise to the BCR-ABL1 fusion gene, and produces a Philadelphia chromosome; the visible result of this translocation.

The presence of a BCR-ABL1 fusion has important diagnostic and prognostic implications in a number of haematological disorders.

The t(9;22)(q34.12;q11.23) translocation is the hallmark of chronic myeloid leukaemia (CML) and is found in around 90-95%[1] of cases. The remaining cases have a variant translocation, or have a cryptic translocation between 9q34 and 22q11.23 that cannot be identified by routine cytogenetic analysis[1]. BCR-ABL1 fusions can also be found in 25% of adult acute lymphoblastic leukaemia (ALL) and in 2-4% of childhood ALL[1]. This rearrangement is also seen in rare cases of acute myeloid leukaemia (AML)[2].

The translocation between chromosomes 9 and 22 can be accompanied by loss of proximal sequences on the derivative chromosome 9, including the ASS1 region[3]. Concomitant ASS1 gene deletions have been associated with poorer prognosis in CML, although this may be partially abrogated by treatment with TKIs[4]; therefore, the establishment of atypical patterns in patients with the BCR-ABL1 translocation may have clinical diagnostic and prognostic implications.



** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

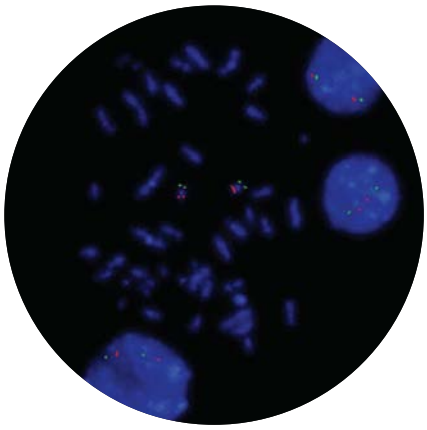
REFERENCES

1. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France, IARC:2008
2. Soupir *et al*., Am J Clin Pathol 2007;127:642-650
3. Robinson *et al*., Leukemia 2005;19(4):564-71
4. Siu *et al*., BMC Blood Disorders 2009;9:4

Cytocell an OGT company aquarius

Cat. No. **LPH 022-S** (5 tests)
Cat. No. **LPH 022** (10 tests)

CBFβ/MYH11 Translocation, Dual Fusion



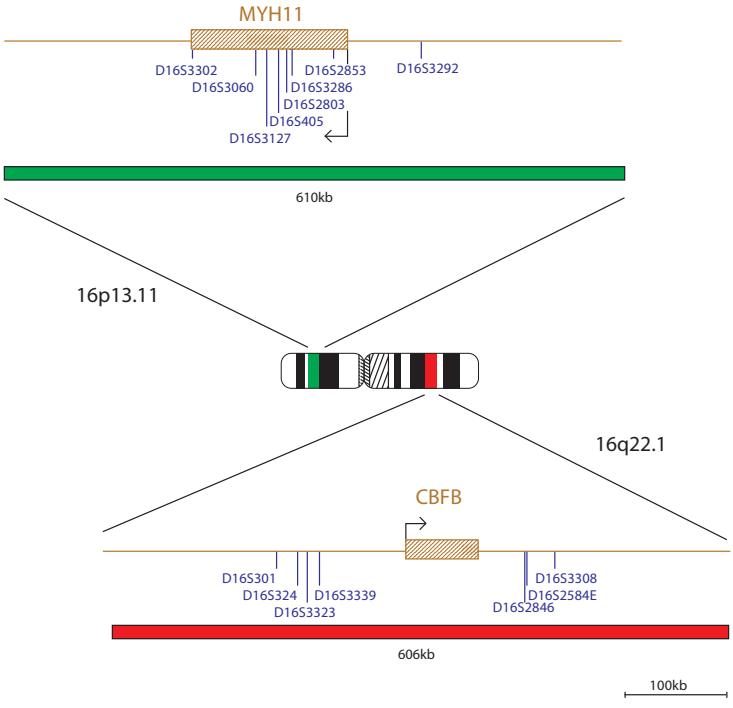
AML **

The CBFB (*core-binding factor, beta subunit*) gene is located at 16q22.1 and the MYH11 (*myosin, heavy chain 11, smooth muscle*) gene is located at 16p13.11. The inversion inv(16)(p13.11;q22.1) and the translocation t(16;16)(p13.11;q22.1) give rise to the CBFB-MYH11 fusion gene.

Acute myeloid leukaemias with inv(16)(p13.11;q22.1) or t(16;16)(p13.11;q22.1) form a recognised disease entity according to the World Health Organization (WHO) classification of myeloid neoplasms and acute leukaemia[1]. These rearrangements are frequently found in patients with a myelomonocytic subtype with increased bone marrow eosinophils, AML FAB (French-American-British classification) type M4Eo, and are found in 5-8%[1] of all AMLs. Cases of therapy-related AML may also have this rearrangement[1,2].

CBFB-MYH11 rearrangements are classed as a favourable cytogenetic risk group in patients with AML[3,4].

The breakpoints occur in intron 5 of CBFB and intron 5 of MYH11. The N-terminal of CBFB fuses to the C-terminal of MYH11 with its multimerisation domain. The resultant chimaeric protein reduces the amount of active CBF. An accumulation of CBFB-MYH11/CBFA multimers in the nucleus also occurs. CBFB regulates expression of certain ADP-ribosylation factors (ARFs) and other tumour suppressor genes (TSGs) and therefore the fusion protein is thought to repress TSG expression[3].



REFERENCES

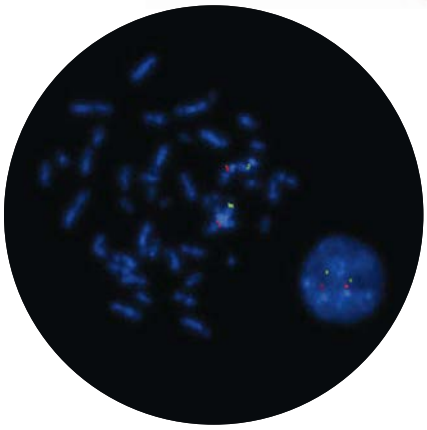
1. Swerdlow *et al*., editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France,IARC:2008
2. Hernández et al., Haematologica 2000;85(5):481-5.
3. Moreno-Miralles *et al*., J Biol Chem 2005;280(48):40097-103
4. Grimwade *et al*., Blood 2010;116(3):354-365

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 039-S** (5 tests)
Cat. No. **LPH 039** (10 tests)

CKS1B/CDKN2C (P18) Amplification/Deletion



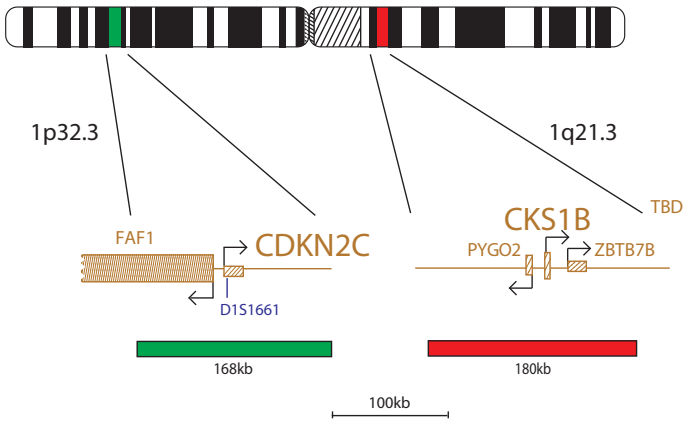
MM **

The CKS1B (*CDC28 protein kinase regulatory subunit 1B*) gene is located at 1q21.3 and the CDKN2C (*P18, cyclin-depended kinase inhibitor 2C [p18, inhibits CDK4]*) gene is located at 1p32.3.

Gain of the 1q21 region including CKS1B is one of the most frequently-occurring chromosomal aberrations seen in multiple myeloma[1]. Over-expression of the CKS1B gene up-regulates cell cycle progression, resulting in a more proliferative disease[2]. This is related to the advanced phenotype of multiple myeloma and may therefore be associated with poor prognosis and disease progression[1,2,3]. Gain of 1q21 has been linked to inferior survival and further amplification is observed in disease relapse. Complete gains of the long arm of chromosome 1 are also common in multiple myeloma and can occur as isochromosomes, duplications or jumping translocations and are frequently associated with disease progression[4].

CDKN2C is a tumour suppressor gene responsible for inducing apoptotic cell death and DNA fragmentation[5]. It is up-regulated by the expression of the cytokine IL-6 in multiple myeloma and homozygous deletion of the gene is associated with a more proliferative disease[5]. Although CDKN2C deletions have been reported to be rare in human malignancy, cytogenetic analyses have shown that abnormalities of 1p32-36 occur in around 16% of human multiple myeloma and are associated with worse overall survival[2,3,5,6].

Cytogenetic abnormalities are detected by conventional cytogenetics in about one third of cases of multiple myeloma, but FISH increases the proportion of chromosomal abnormalities to >90%[7].



REFERENCES

1. Hanamura I, Blood 2006;108(5):1724-32
2. Fonseca *et al*., Leukemia 2009;23(12):2210-2221
3. Sawyer, Cancer Genetics 2011;204(1):3-12
4. Fonseca *et al*., Leukemia 2006;20(11):2034-40
5. Leone *et al*., Clin Cancer Res. 2008;14(19):6033-41
6. Kulkarni *et al*., Leukemia 2002;16:127-34
7. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France, IARC:2008

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 067-S** (2x5 tests)
Cat. No. **LPH 067** (2x10 tests)

CLL PROFILER Kit

The Cytocell CLL PROFILER Kit is intended to detect deletions of TP53, ATM and D13S319, and gains of the chromosome 12 centromere sequences in peripheral blood or bone marrow samples from patients with chronic lymphocytic leukaemia (CLL).

P53 (TP53)/ATM Probe Combination

The TP53 (*tumor protein p53*) gene at 17p13.1 is one of most important tumour suppressor genes; it acts as a potent transcription factor with fundamental role in the maintenance of genetic stability. Loss of TP53 is reported in 10% of patients with CLL, and is considered to be the poorest prognostic marker in that disease[1,2]. The ATM (*ataxia-telangiectasia mutated*) gene at 11q22.3 is an important checkpoint gene involved in the management of cell damage and its function is to assess the level of DNA damage in the cell and attempt repair by phosphorylating key substrates involved in the DNA damage response pathway[3]. Loss of ATM is reported in 18% of patients with CLL, and is considered a poor prognostic marker in that disease[4]. Analysis of the ATM/TP53 interaction in CLL has shown that TP53 and ATM play an important role in the proliferation of lymphoid cancer[3]. It has been shown that ATM enhances the phosphorylation of TP53, should the damage be so great that the cell requires destruction by apoptosis (which is mediated by TP53). Deletion of ATM removes this checkpoint activity and hence activation of TP53. Thus, there is no attempt made to repair, or apoptosis of, damaged cells, despite the presence of TP53. In the absence of ATM, damaged cells are allowed to continue to proliferate[5].

D13S319/13qter/12cen Deletion/Enumeration

Deletions affecting 13q14 are also the most frequent structural genetic aberrations in chronic lymphocytic leukaemia (CLL)[6,7,8]. This region is found to be heterozygously deleted in 30-60% and homozygously deleted in 10-20% of CLL patients[9]. The survival rate has been shown to be similar for the two groups[10]. Patients with 13q14 deletions are classified as very low risk, in the absence of any other genetic lesions[1]. Two non-coding RNA genes, DLEU1 (*deleted in lymphocytic leukemia 1*) and DLEU2 (*deleted in lymphocytic leukemia 2*), plus the genetic marker D13S319, span the pathogenic critical region of 13q14[11]. DLEU1 is considered to be the most likely CLL-associated candidate tumour suppressor gene within the 13q14 region[12]. Trisomy 12 is a recurrent abnormality in CLL, seen in 20% of the cases[13] and often appears as the unique cytogenetic aberration (40-60% of cases with trisomy 12)[7]. Patients with trisomy 12 are classified as low-risk in the absence of any other genetic lesions[1].

REFERENCES

1. Rossi D, *et al*. Blood. 2013 Feb 21;121(8):1403-12
2. Baliakas P, *et al*. Leukemia. 2014;(April):1-8
3. Stankovic *et al*., Blood 2004;103(1):291-300
4. Dohner *et al*., N Eng J Med 2000;343:1910-1916
5. Khanna *et al*., Nature Genetics 1998;20(4):398-400
6. Juliusson G *et al*., N Eng J Med 1990;323:720-4
7. Puiggros *et al*., Biomed Res Int 2014;1-13
8. Kasar *et al*., Nature Communications 2015;6:1-12
9. Hammarsund M *et al*., FEBS Letters 2004;556:75-80
10. Van Dyke DL *et al*., Br J Haematology 2009;148:544-50
11. Liu Y *et al*., Oncogene 1997;15:2463-73
12. Wolf S *et al*., Hum Mol Genet 2001;10:1275-85
13. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon, France, IARC:2008

Cytocell an OGT company aquarius

Cat. No. **LPH 087-S** (5x5 tests)
Cat. No. **LPH 087** (5x10 tests)

CLL *Plus* Screening Panel

A selection of haematology probes and an alpha-satellite probe for chronic lymphocytic leukaemia (CLL).

Alpha Satellite 12 *Plus* for CLL

Trisomy 12 is a recurrent abnormality in CLL, seen in 20% of cases[1] that often appears as the unique cytogenetic aberration (40-60% of cases with trisomy 12)[2]. Patients with trisomy 12 are classified as low-risk in the absence of any other genetic lesions[3]. This product is also available in 5 (LPH 069-S) and 10 (LPH 069) test kit sizes and has been optimised for overnight hybridisation.

13q14.3

Deletions affecting 13q14 are the most frequent structural genetic aberrations in CLL[4,5,6]. This region is found to be heterozygously deleted in 30-60% and homozygously deleted in 10-20% of CLL patients[7]. Patients with 13q14 deletions are classified as very low risk, in the absence of any other genetic lesions[3].

P53 (TP53) (17p13.1)

The TP53 (*tumor protein p53*) gene at 17p13.1 is one of most important tumour suppressor genes; it acts as a potent transcription factor with fundamental role in the maintenance of genetic stability. Loss of TP53 is reported in 10% of patients with CLL, and is considered to be the poorest prognostic marker[3,8].

ATM (11q22.3)

The ATM (*ataxia-telangiectasia mutated*) gene at 11q22.3 is an important checkpoint gene involved in the management of cell damage and its function is to assess the level of DNA damage in the cell and attempt repair by phosphorylating key substrates involved in the DNA damage response pathway[9]. Loss of ATM is reported in 18% of patients with CLL, and is considered a poor prognostic marker in CLL[10].

MYB (6q23.3)

Deletions of chromosome 6q are recurrent in CLL. The MYB (*v-myb avian myeloblastosis viral oncogene homolog*) gene is essential in haematopoietic cell proliferation and differentiation[11,12]. It is located in band 6q23.3 and is provided as a marker for 6q deletion.

REFERENCES

1. Swerdlow *et al.*,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France, IARC:2008
2. Puiggros *et al.*, Biomed Res Int 2014;1-13
3. Rossi *et al.*, Blood 2013;121(8):1403-1412
4. Juliusson G *et al.*, N Eng J Med 1990;323:720-4
5. Puiggros *et al.*, Biomed Res Int 2014;1-13
6. Kasar *et al.*, Nature Communications 2015;6:1-12
7. Hammarsund M *et al.*, FEBS Letters 2004;556:75-80
8. Baliakas P, *et al*. Leukemia. 2014;(April):1-8
9. Stankovic *et al.*, Blood 2004;103(1):291-300
10. Dohner *et al.*, N Eng J Med 2000;343:1910-1916
11. Clappier *et al.*, Blood 2007;110(4):1251-1261
12. Stilgenbauer *et al.*, Leukemia,1999;13:1331-1334

Cytocell an OGT company aquarius

Cat. No. **LPH 010-S** (5 tests)
Cat. No. **LPH 010** (10 tests)

cMYC (MYC) Breakapart*

L **

Chromosomal rearrangements involving the MYC (*v-myc avian myelocytomatosis viral oncogene homolog*) gene at 8q24 are recognised recurrent abnormalities commonly seen in patients with B-cell malignancy.

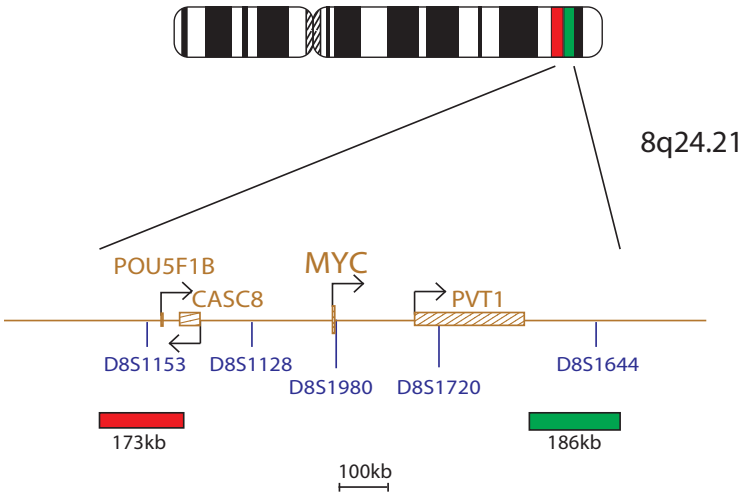
MYC rearrangements, activating MYC by translocation with one of the three immunoglobulin loci (IGH, IGL or IGK), are detected in almost all cases of Burkitt lymphoma at diagnosis[1]. They are also seen in diffuse large B-cell lymphoma (DLBCL)[2], multiple myeloma and plasmablastic lymphomas[3,4], amongst other diseases.

MYC has also been shown on rare occasions to be involved in rearrangements with a number of non-immunoglobulin partners[5].

The presence of concurrent MYC rearrangements with BCL2 and/or BCL6 rearrangements in patients with 'dual-hit' lymphoma has been shown to be associated with aggressive disease[6].

REFERENCES

1. Perkins AS, Friedberg JW. Hematology Am Soc Hematol Educ Program. 2008;341-8
2. Ott G, *et al*. Blood. 2013 Dec 5;122(24):3884-91
3. Walker BA, *et al*. Blood Cancer J. 2014;4(3)
4. Elyamany G, *et al*. Adv Hematol 2015;2015:315289
5. Bertrand P, *et al*. Leukemia 2007;21:515-23
6. Aukema SM, *et al*. Blood. 2011; Feb 24;117(8):2319-31



*** A similar product is also available within the Haematopathology range, refer to page 93.**

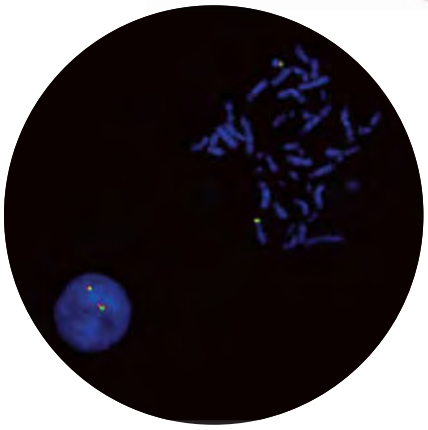
** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **RU-LPH 085-S†** (50µl) | Cat. No. **RU-LPH 086-S†** (50µl)

Cat. No. **RU-LPH 085†** (100µl) | Cat. No. **RU-LPH 086†** (100µl)

CRLF2 Breakapart† and P2RY8 Deletion†



ALL **

CRLF2 (*cytokine receptor-like factor 2*) at Xp22.33/Yp11.3 has been shown to be overexpressed in B-cell acute lymphoblastic leukaemia (B-ALL).

CRLF2 overexpression has been shown to be caused by chromosomal rearrangements such as the t(X;14)(p22;q32) or t(Y;14)(p11;q32) translocations or, alternatively, via interstitial deletions of the pseudoautosomal region 1 (PAR1) of chromosomes X and Y, which includes the P2RY8 (*purinergic receptor P2Y8*) gene. These place CRLF2 under control of an IGH enhancer[1] or juxtapose the first non-coding exon of P2RY8 to the coding region of CRLF2[2], respectively. All these CRLF2 rearrangements are cytogenetically cryptic and cannot be detected by conventional G-banded analysis[1], making FISH a powerful detection tool for these abnormalities.

Overexpression of CRLF2 has been associated with activation of the JAK/STAT5 pathway in transduced primary B-cell progenitors[1,3] and various groups have attempted to characterise the biochemical consequences of these genetic lesions, with the goal of identifying targets for new therapies[2,3].

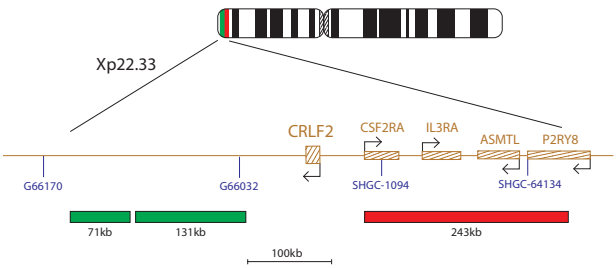
Rearrangements of CRLF2 can be found in 6% of childhood and adult B-ALL, but are more prevalent in Down syndrome ALL (54%)[4]. In B-ALL, gene expression profiling has identified an unusual genetic subgroup, the BCR-ABL1-like or Philadelphia chromosome-like (Ph-like) ALL, which represents about 15%[4,5] of paediatric ALL cases and has an unfavourable outcome. Patients with this expression signature are characterised by genetic alterations, such as rearrangements, mutations and deletions of a range of kinase and cytokine receptors. CRLF2 is rearranged in up to 50%[6] of Ph-like ALLs[4,5,6,7].

The Cytocell CRLF2 breakapart probe will detect rearrangements of the CRLF2 gene, whilst the P2RY8 deletion probe allows detection of deletions between CRLF2 and P2RY8, causing the fusion gene.

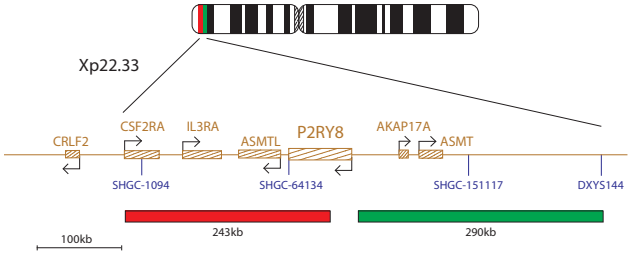
REFERENCES

1. Russell *et al*., Blood. 2009 Sep 24;114(13):2688-2698
2. Mullighan *et al*., Nat Genet 2009; 41(11): 1243-1246
3. Tasian *et al*., Blood 2012; 120(4):833-842
4. Harrison, Hematology Am Soc Hematol Educ Program. 2013;2013:118-125
5. Mullighan, J Clin Invest 2012;122(10):3407-3415
6. Roberts *et al*., Cancer Cell 2012;22(2):153-166
7. Roberts *et al*., N Eng J Med 2014;371(11):1005-1015

CRLF2 Cat. No. **RU-LPH 085***



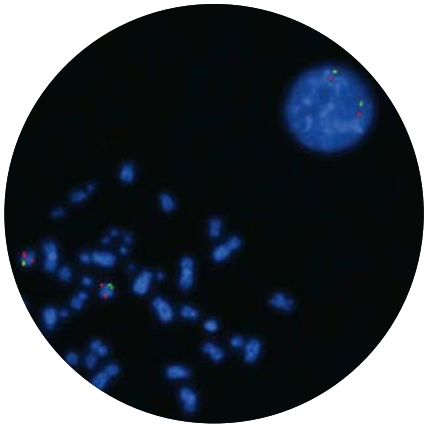
P2RY8 Cat. No. **RU-LPH 086***



† For research use only, not for use in diagnostic procedures.

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Deletion 13q14.3, D13S319 *Plus* and D13S25



13q14.3 Deletion

CLL MM **

Rearrangements leading to the loss of all or part of the long arm of chromosome 13 are seen frequently in a wide range of haematological disorders.

Chromosome 13q aberrations occur in 16-40% of multiple myeloma cases (MM), most of them being complete monosomy 13 (85%), while the remaining 15% constitute deletion of 13q[1,2,3]. A case study of multiple myeloma patients narrowed down the critical deleted region to 13q14[4]. Historically, deletions of 13q have been associated with poor prognosis in MM but now it is believed that its prognostic relevance may be related to its association with other concurrent genetic lesions[3,5].

Deletions affecting 13q14 are also the most frequent structural genetic aberrations in chronic lymphocytic leukaemia (CLL)[6,7,8]. This region is found to be heterozygously deleted in 30-60% and homozygously deleted in 10-20% of CLL patients[9]. The survival rate has been shown to be similar for the two groups[10]. Patients with 13q14 deletions are classified as very low risk, in the absence of any other genetic lesions[11].

Two non-coding RNA genes, DLEU1 (*deleted in lymphocytic leukemia 1*) and DLEU2 (*deleted in lymphocytic leukemia 2*), plus the genetic marker D13S319, span the pathogenic critical region of 13q14[12]. DLEU1 is considered to be the most likely CLL-associated candidate tumour suppressor gene within the 13q14 region[13]. Subsequently, D13S319, located between the RB1 gene and D13S25 and within the DLEU1 locus, was found to be deleted in 44% of CLL cases[14]. It has also been postulated that a gene telomeric to the D13S319 region, encompassing D13S25, may be important in cases with hemizygous deletions and that this gene is a putative tumour suppressor gene[15].

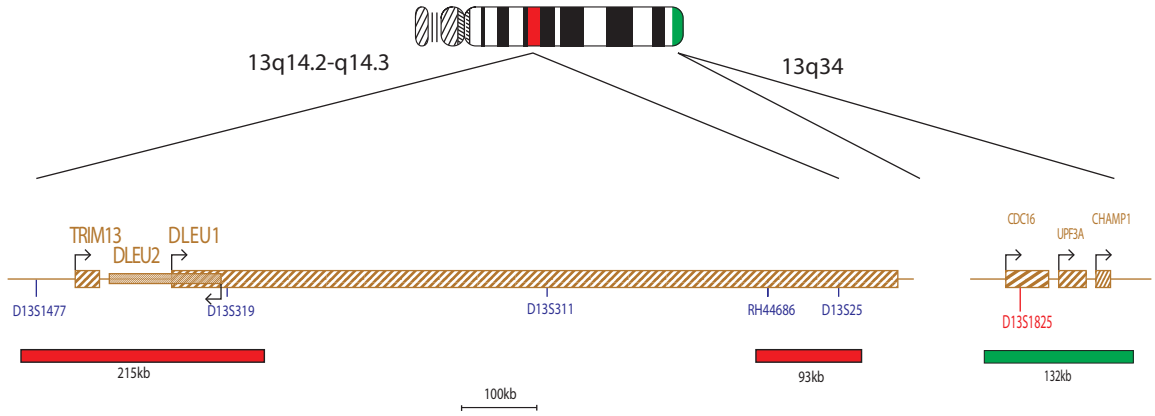
REFERENCES

1. Bullrich F *et al*., Cancer Res 2001;61:6640-8
2. Zojer *et al*., Blood 2000;95(6):1925-1930
3. Sawyer, Cancer Genetics 2011;204:3-12
4. Shaughnessy J *et al*., Blood 2000;96:1505-11
5. Fonseca *et al*., Leukemia 2009;23:2210-2221
6. Juliusson G *et al*., N Eng J Med 1990;323:720-4
7. Puiggros *et al*., Biomed Res Int 2014;1-13
8. Kasar *et al*., Nature Communications 2015;6:1-12
9. Hammarsund M *et al*., FEBS Letters 2004;556:75-80
10. Van Dyke DL *et al*., Br J Haematology 2009;148:544-50
11. Rossi *et al*., Blood 2013;121(8):1403-1412
12. Liu Y *et al*., Oncogene 1997;15:2463-73
13. Wolf S *et al*., Hum Mol Genet 2001;10:1275-85
14. Liu Y *et al*., Blood 1995;86:1911-5
15. Bullrich F *et al*., Blood 1996;88(8):3109-15

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

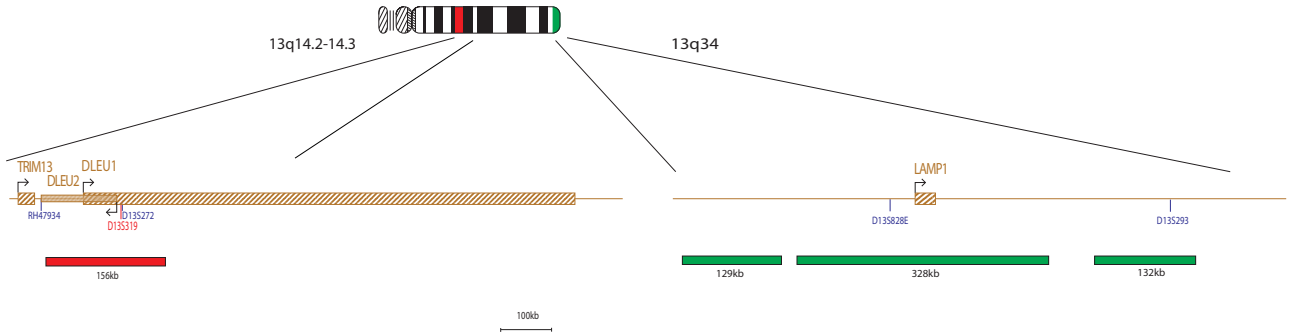
13q14.3

Cat. No. **LPH 006**



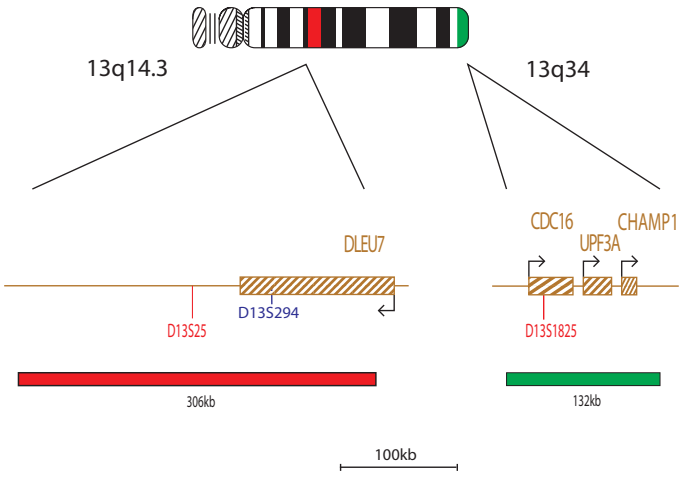
D13S319 *Plus*

Cat. No. **LPH 068**



D13S25

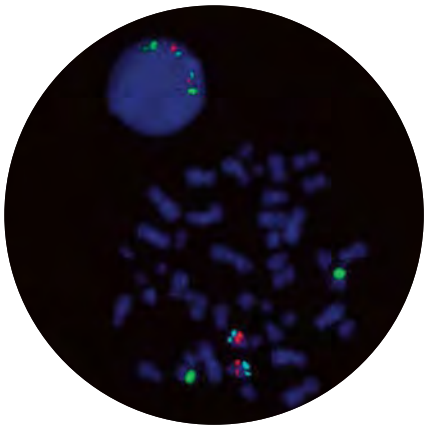
Cat. No. **LPH 043**



Cytocell an OGT company aquarius

Cat. No. **LPH 066-S** (5 tests)
Cat. No. **LPH 066** (10 tests)

D13S319/13qter/12cen Deletion/Enumeration



CLL MM **

Deletions affecting band 13q14 and trisomy of chromosome 12 are common events in chronic lymphocytic leukaemia (CLL).

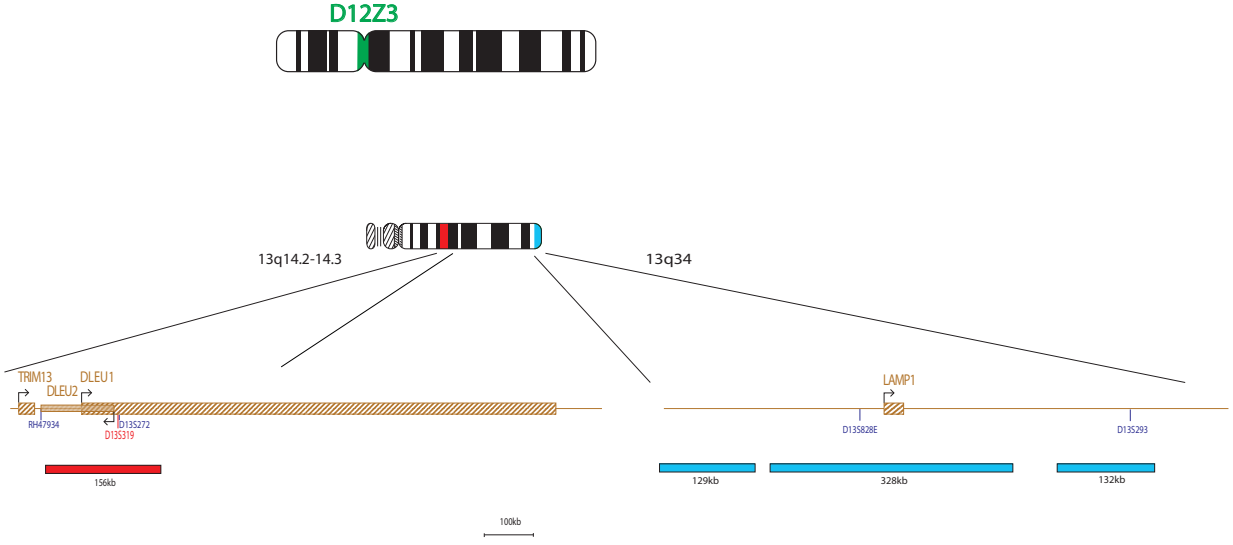
Deletions affecting 13q14 are also the most frequent structural genetic aberrations in chronic lymphocytic leukaemia (CLL)[1,2,3]. This region is found to be heterozygously deleted in 30-60% and homozygously deleted in 10-20% of CLL patients[4]. The survival rate has been shown to be similar for the two groups[5]. Patients with 13q14 deletions are classified as very low risk, in the absence of any other genetic lesions[6].

Two non-coding RNA genes, DLEU1 (*deleted in lymphocytic leukemia 1*) and DLEU2 (*deleted in lymphocytic leukemia 2*), plus the genetic marker D13S319, span the pathogenic critical region of 13q14[7]. DLEU1 is considered to be the most likely CLL-associated candidate tumour suppressor gene within the 13q14 region[8].

Trisomy 12 is a recurrent abnormality in CLL, seen in 20% of the cases[9] and often appears as the unique cytogenetic aberration (40-60% of cases with trisomy 12)[2]. Patients with trisomy 12 are classified as low-risk in the absence of any other genetic lesions[6].

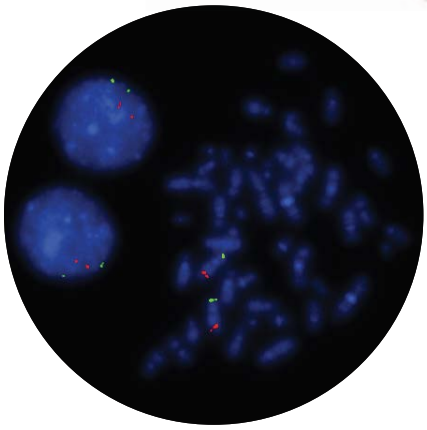
REFERENCES

1. Juliusson G *et al*., N Eng J Med 1990;323:720-4
2. Puiggros *et al*., Biomed Res Int 2014;1-13
3. Kasar *et al*., Nature Communications 2015;6:1-12
4. Hammarsund M *et al*., FEBS Letters 2004;556:75-80
5. Van Dyke DL *et al*., Br J Haematology 2009;148:544-50
6. Rossi *et al*., Blood 2013;121(8):1403-1412
7. Liu Y *et al*., Oncogene 1997;15:2463-73
8. Wolf S *et al*., Hum Mol Genet 2001;10:1275-85
9. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon, France, IARC:2008



** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Del(5q) Deletion



AML MDS MPN **

Deletions of the long arm of chromosome 5 are one of the most common karyotypic abnormalities in myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML) with myelodysplasia related changes[1,2].

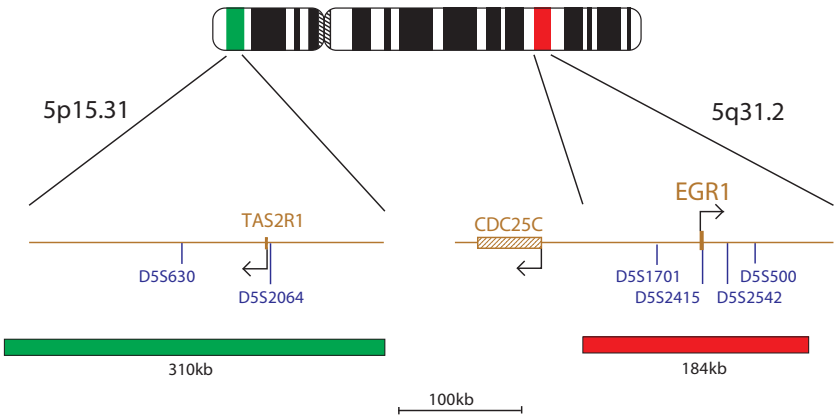
A subset of patients with del(5q) as a sole cytogenetic abnormality has a consistent set of clinical features, termed the 5q- syndrome[1]. This clinical entity with <5% blasts has a more favourable prognosis and responds to treatment with lenalidomide. However, patients with del(5q) associated with other cytogenetic abnormalities or with excess blasts have an inferior survival[2,3].

Two chromosomal regions have been mapped on chromosome 5q in MDS. One common deleted region, at 5q33, is associated with the 5q-syndrome. Another, more proximal region, located at 5q31, has been linked to a more aggressive form of MDS and AML and is often accompanied by additional cytogenetic abnormalities and a poorer prognosis[1,3,4,].

The Cytocell del(5q) probe will detect deletions of EGR1 (*early growth response 1*), a tumor suppressor gene at 5q31. EGR1 has been shown to act through haploinsufficiency to initiate the development of MDS/AML[5].

REFERENCES

1. Ebert, Best Pract Res Clin Haematol 2010;23(4):457-461
2. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon, France, IARC:2008
3. Fang *et al*., Cell Reports 2014;8(5):1328-1338
4. Boultwood *et al*., Blood;116(26):5803-5811
5. Joslin *et al*., Blood;110(2):719-726

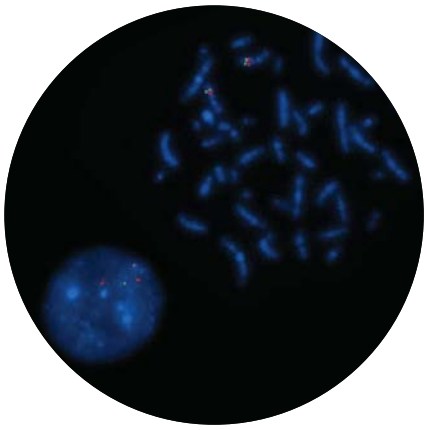


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 025-S** (5 tests)
Cat. No. **LPH 025** (10 tests)

Del(7q) Deletion



AML MDS MPN **

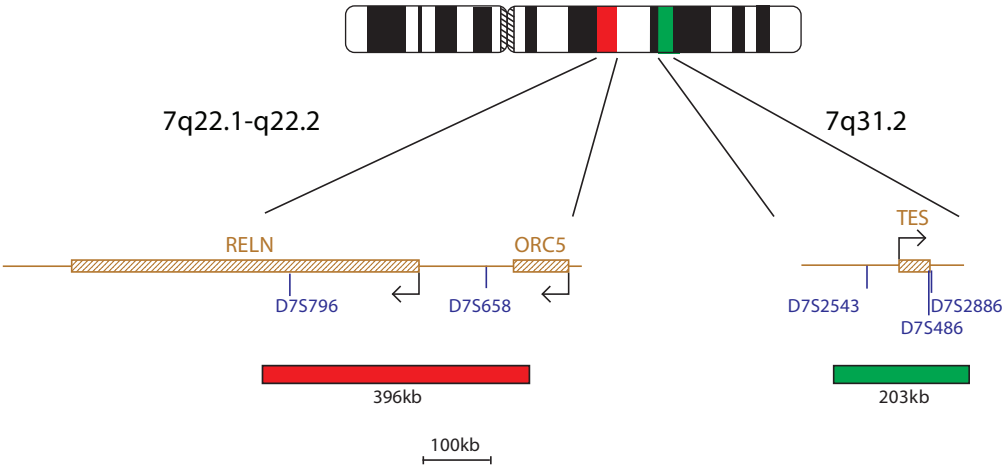
Monosomy of chromosome 7 and deletions of the long arm of chromosome 7 are recognised recurrent chromosomal aberrations frequently seen in myeloid disorders.

Monosomy 7 and del(7q) are seen a number of myeloid disorders, including myelodysplastic syndrome (MDS), acute myeloid leukaemia (AML), and juvenile myelomonocytic leukemia (JMML)[1]. Furthermore, it occurs in MDS and AML that develop in patients with constitutional disorders (eg, Fanconi anaemia, Kostmann syndrome, neuro-fibromatosis type 1, and familial monosomy 7)[2]. The presence of monosomy 7 or del(7q) as karyotypic changes are associated with a poorer outcome in myeloid malignancies[1,3].

Deletions of chromosome 7 are typically large with heterogeneity in the breakpoints in myeloid diseases, making it difficult to map the common deleted regions (CDRs). It is highly likely that multiple tumour suppressor genes on chromosome 7 cooperate in leukaemogenesis[4]. Two CDRs have been previously reported: one at 7q22 and the other on 7q31-q36[2,5], which are both targeted by this probe set.

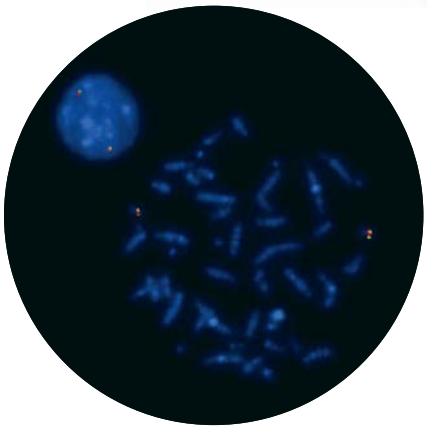
REFERENCES

1. Jerez *et al*., Blood 2012;119(25):6109-6118
2. Fisher *et al*., Blood 1997;89(6):2036-2041
3. Trobaugh-Lotrario et al., Bone Marrow Transplantation 2005;35(2):143-149
4. McNerney *et al*., Blood 2013;121(6):975-983
5. Thoennissen *et al*., American J Haem 2011;86(8):699-701



** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Del(20q) Deletion



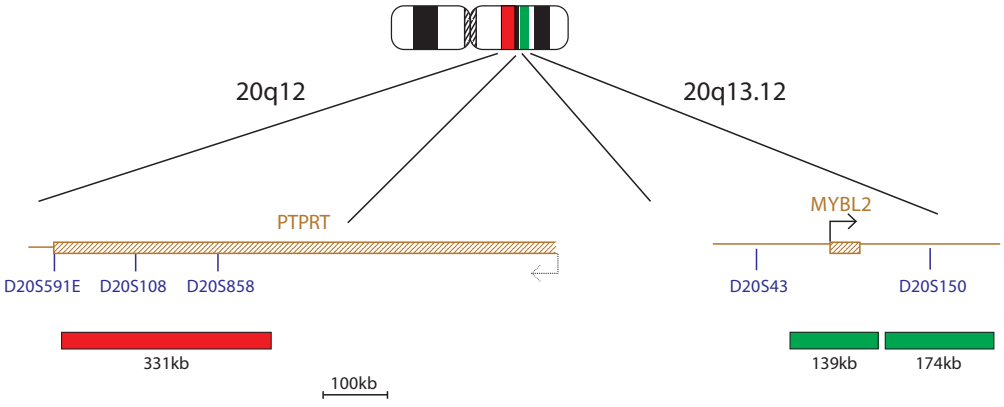
AML MDS MPN **

Deletions of the long arm of chromosome 20 are a common chromosomal abnormality associated with myeloid malignancies, in particular myeloproliferative neoplasms (MPN), myelodysplastic syndromes (MDS) and acute myeloid leukaemia (AML)[1].

Deletion of the long arm of chromosome 20 [del(20q)] is observed in 10% of patients with polycythemia vera (PV) and in other MPNs[2]. Additionally it can be seen in 4% of MDS cases and in 1-2% of AML cases[2]. The prognosis for MDS where del(20q) is the sole abnormality is good; however, the presence of secondary abnormalities may be indicative of disease progression[3].

FISH is particularly useful in confirming the presence and extent of the abnormality in poor cytogenetic sample preparations.

Potential target genes have been investigated in the region of overlap between the AML/MDS and MPD common deleted region at band 20q12. Five genes were expressed in both bone marrow and CD34+ cells. Of these genes, three were previously identified: L3MBTL1 regulates chromatin structure during mitosis; SRSF6 encodes a serine rich protein important to regulation of alternative splicing of mRNA; and MYBL2, a member of the MYB transcription factor family, is involved in cell cycle control[2,4,5].



REFERENCES

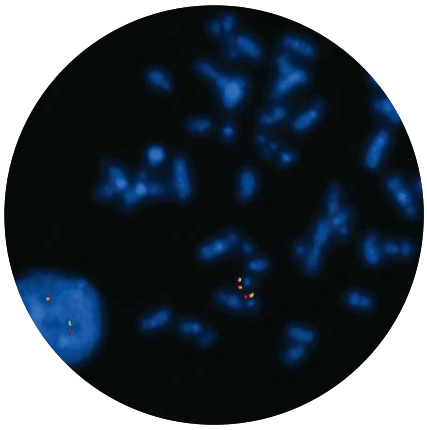
1. Březinová *et al*., 2005:160(2):188-192
2. Bench *et al*., Oncogene 2000;19(34):3902-13
3. Liu *et al*., Cancer Genet Cytogenet. 2006 Nov;171(1):9-16
4. Li J *et al*., PNAS 2004;101:7341-6
5. Wang *et al*., Genomics 1999;59:275-81

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 019-S** (5 tests)
Cat. No. **LPH 019** (10 tests)

E2A (TCF3) Breakapart



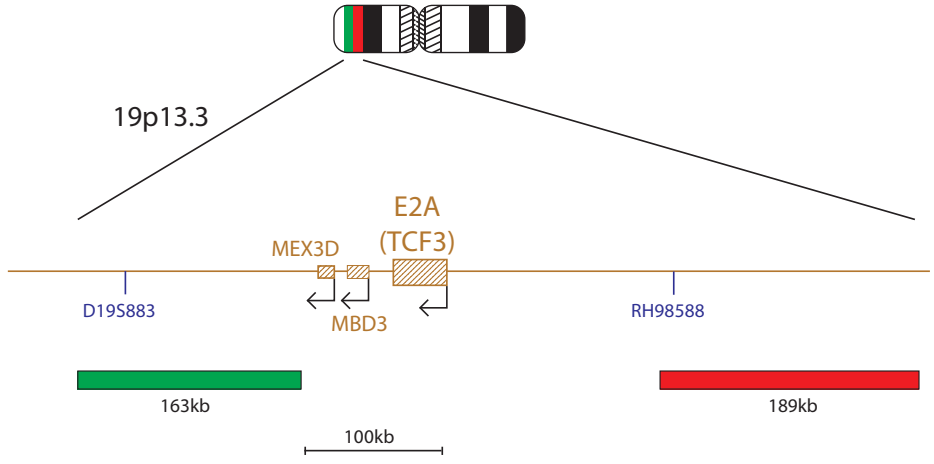
ALL **

The TCF3 (*transcription factor 3*) gene is located at 19p13.3. Translocations involving TCF3 are some of the most common rearrangements in childhood B-cell acute lymphoblastic leukaemia (ALL)[1,2].

Two of the main TCF3 partners are PBX1 (*pre-B-cell leukemia homeobox 1*) at 1q23.3 and HLF (*hepatic leukemia factor*) at 17q22. These become fused to TCF3 as a result of the t(1;19)(q23;p13) and t(17;19)(q22;p13) translocations, forming the TCF3-PBX1 and TCF3-HLF fusion genes, respectively. A rare cryptic inversion, inv(19)(p13;q13), has been reported to fuse TCF3 to TFPT (*TCF[E2A] fusion partner [in childhood leukaemia]*), resulting in the TCF3-TFPT fusion gene[1].

The t(1;19)(q23;p13) is the most common TCF3 rearrangement, being present in around 6% of childhood B-ALL[1,2]. According to the World Health Organization (WHO) classification of myeloid neoplasms and acute leukaemia, B lymphoblastic leukaemia/lymphoma with t(1;19)(q23;p13); TCF3-PBX1 is recognised as a distinct disease entity[2]. The functional fusion gene resides at chromosome 19. An unbalanced form of this translocation has been reported, with loss of der(1)[1,2]. Detection of the E2A-PBX1 fusion by molecular methods, such as FISH, is important, as a subset of B-ALLs has a karyotypically identical t(1;19) that involves neither TCF3 nor PBX1. E2A-PBX1 positive leukaemia was historically associated with a poor outcome, though modern intensive therapies have overcome this[1,2,4].

The t(17;19)(q22;p13.) is a rare translocation that is present in around 1% of precursor B-ALL cases[1]. TCF3-HLF positive leukaemia is associated with adverse prognosis[3,4].

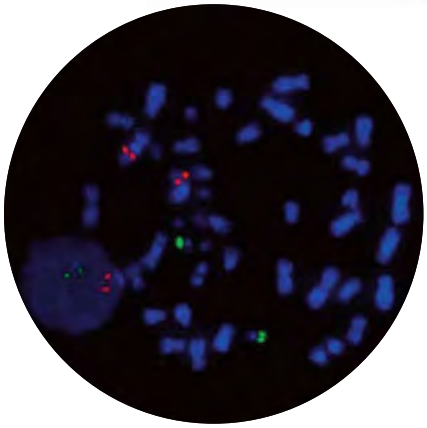


REFERENCES

1. Van der Burg *et al*., Leukemia 2004;18(5):895-908
2. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon, France, IARC:2008
3. Mullighan, The Journal of Clinical Investigation 2012;122(10):3407-3415
4. Moorman *et al*., Lancet Oncol Haematol. January 2012

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

E2A (TCF3)/PBX1 Translocation, Dual Fusion

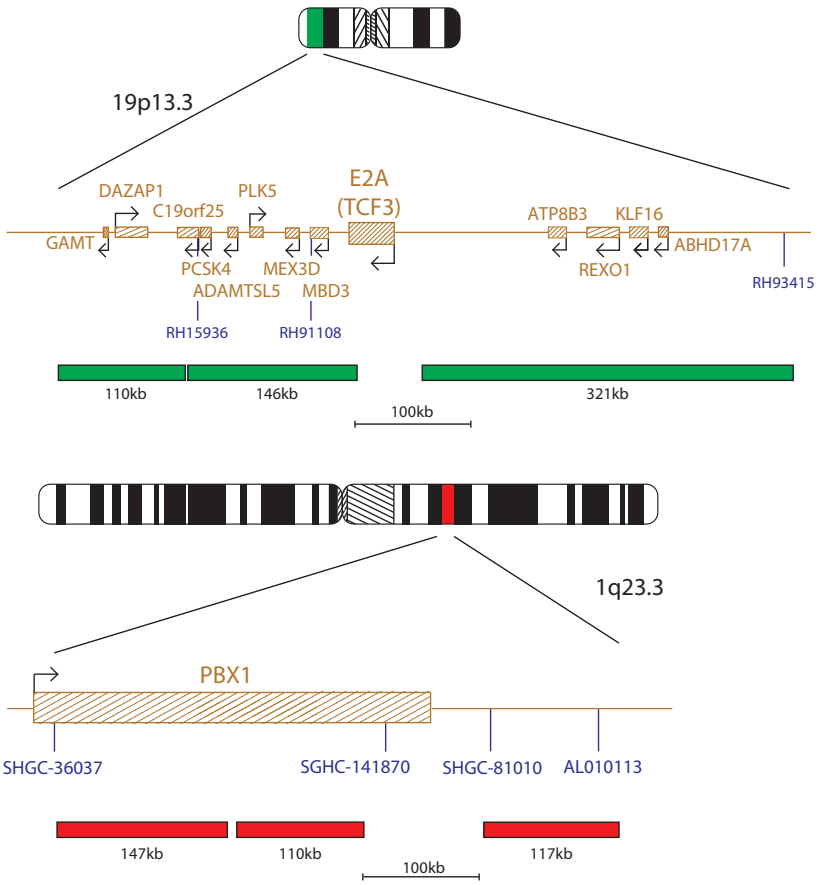


ALL **

The TCF3 (*transcription factor 3*) gene is located at 19p13.3 and PBX1 (*pre-B-cell leukemia homeobox 1*) at 1q23.3. Translocations involving TCF3 are some of the most common rearrangements in childhood B-cell acute lymphoblastic leukaemia (ALL)[1,2].

Two of the main TCF3 partners are PBX1 at 1q23.3 and HLF at 17q22. These become fused to TCF3 as a result of the t(1;19)(q23;p13) and t(17;19)(q22;p13) translocations, forming the TCF3-PBX1 and TCF3-HLF fusion genes, respectively. A rare cryptic inversion, inv(19)(p13;q13), has been reported to fuse TCF3 to TFPT (*TCF3 [E2A] fusion partner [in childhood leukaemia]*), resulting in the TCF3-TFPT fusion gene[1].

UK and European best practice guidelines both suggest that when a TCF3 rearrangement is identified in B-cell ALL, it is important to distinguish between t(17;19)(q22;p13) and t(1;19)(q23;p13) as the former translocation is associated with adverse prognosis[3,4].



REFERENCES

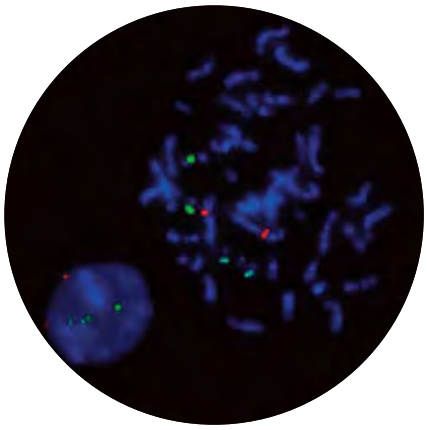
1. Van der Burg *et al*., Leukemia 2004;18(5):895-908
2. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon, France, IARC:2008
3. Professional Guidelines for Clinical Cytogenetics: Acute Lymphoblastic Leukaemia Best Practice Guidelines (2011) V1.00. www.cytogenetics.org.uk
4. Hastings *et al*.,Guidelines and Quality Assurance for Acquired Cytogenetics (2013) ECA Newsletter:31

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 080-S** (5 tests)
Cat. No. **LPH 080** (10 tests)

E2A (TCF3)/PBX1/HLF Translocation, Dual Fusion



ALL **

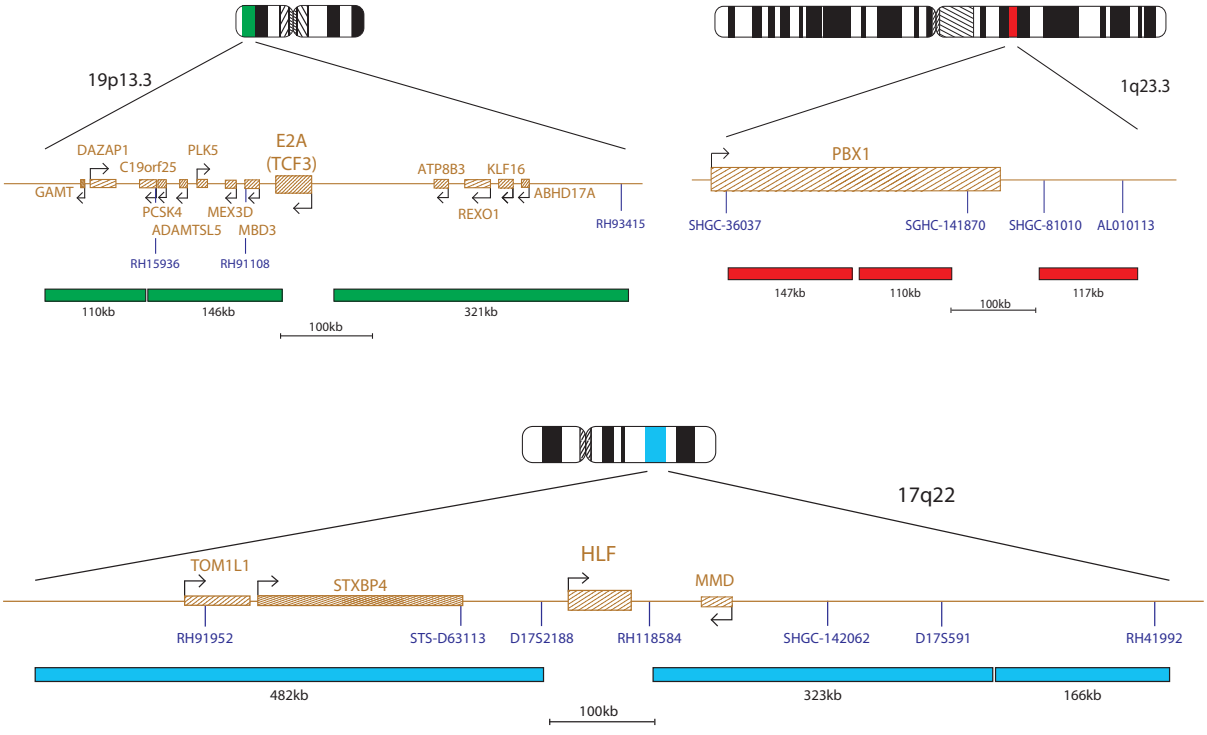
The TCF3 (*transcription factor 3*) gene is located at 19p13.3, PBX1 (*pre-B-cell leukemia homeobox 1*) gene is located at 1q23.3 and HLF (*hepatic leukemia factor*) at 17q22. Translocations involving TCF3 are some of the most common rearrangements in childhood B-cell acute lymphoblastic leukaemia (ALL)[1,2].

PBX1 and HLF become fused to TCF3 as a result of the t(1;19)(q23;p13) and t(17;19)(q22;p13) translocations, forming the TCF3-PBX1 and TCF3-HLF fusion genes, respectively. A rare cryptic inversion, inv(19)(p13;q13), has been reported to fuse TCF3 to TFPT *(TCF3[E2A] fusion partner [in childhood leukaemia])*, resulting in the TCF3-TFPT fusion gene[1].

UK and European best practice guidelines both suggest that when a TCF3 rearrangement is identified in B-cell ALL, it is important to distinguish between t(17;19)(q22;p13) and t(1;19)(q23;p13) as the former translocation is associated with adverse prognosis[3,4].

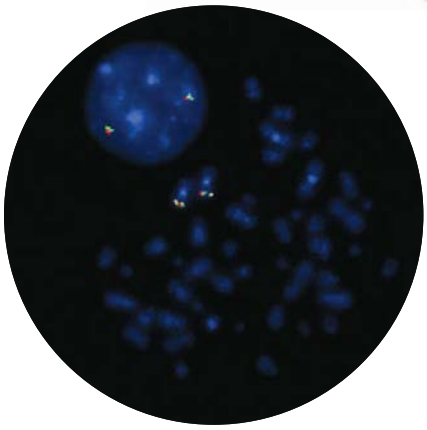
REFERENCES

1. Van der Burg *et al*., Leukemia 2004;18(5):895-908
2. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon, France, IARC:2008
3. Professional Guidelines for Clinical Cytogenetics: Acute Lymphoblastic Leukaemia Best Practice Guidelines (2011) V1.00. www.cytogenetics.org.uk
4. Hastings *et al*.,Guidelines and Quality Assurance for Acquired Cytogenetics (2013) ECA Newsletter:31



** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

EVI1 (MECOM) Breakapart



AML MDS **

The MECOM (*MDS1 and EVI1 complex locus*) oncogene at 3q26.2 is often rearranged in haematological malignancies of myeloid origin.

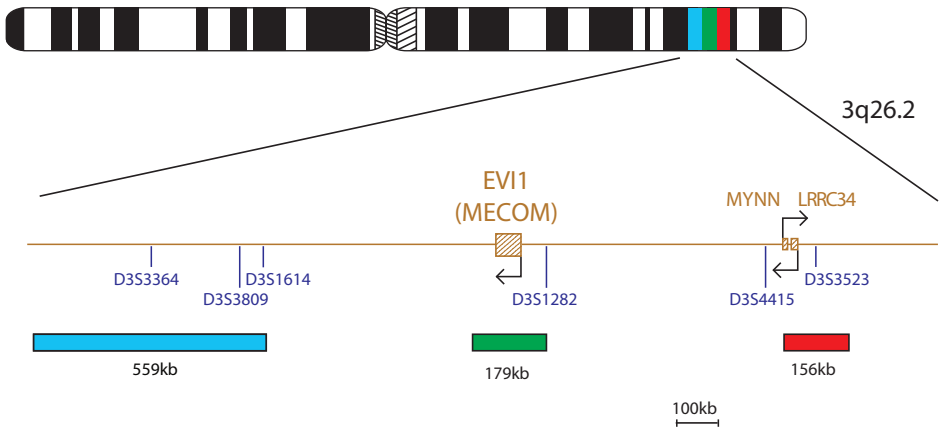
MECOM encodes a zinc finger protein that is inappropriately expressed in the leukaemic cells of between 2-5% of AML and MDS patients[1]. This deregulated expression is often due to a chromosomal rearrangement involving 3q26.2, with the two most common aberrations being the t(3;3)(q21;q26.2) and inv(3)(q21q26.2)[1]. The breakpoints for the translocations and inversions vary considerably. Inversion breakpoints are found centromeric to, and including, the MECOM gene and cover about 600kb. The majority of breakpoints in 3q26.2 translocations are telomeric to the MECOM gene and cover a region including the telomeric end of the MDS1 gene and the MYNN gene[2].

Chromosome rearrangements involving the 3q26.2 region are associated with myeloid malignancies, aberrant expression of MECOM gene, an unfavourable prognosis and an aggressive clinical course[2].

AML with inv(3)(q21q26.2) or t(3;3)(q21;q26.2) is a recognised disease entity according to the World Health Organization (WHO) classification of myeloid neoplasms and acute leukaemia. This is a transformed or *de novo* AML with a very aggressive clinical course and aberrations that involve MECOM at 3q26.2 and RPN1 (*ribophorin I*) at 3q21[3].

MECOM has also been shown to be rearranged in therapy-related disease via the t(3;21)(q26.2;q22) translocation, resulting in a MECOM-RUNX1 fusion[3,4].

MECOM rearrangements are very heterogeneous and may be difficult to detect by conventional cytogenetics, making FISH a useful tool for their detection.



** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

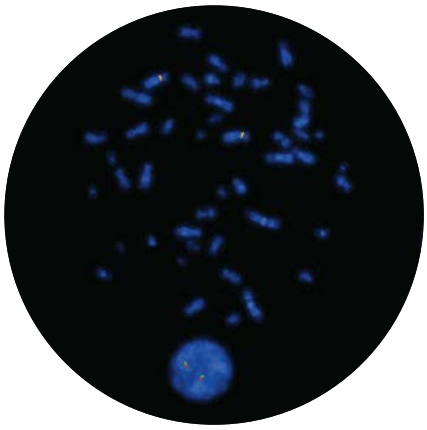
REFERENCES

1. Soderholm *et al*., Leukemia 1997;11:352-358
2. Bobadilla *et al*., Br J Haematol 2007;136:806-813
3. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon, France, IARC:2008
4. Pedersen-Bjergaard *et al*., Leukemia 2008;22:240-248

Cytocell an OGT company aquarius

Cat. No. **LPH 032-S** (5 tests)
Cat. No. **LPH 032** (10 tests)

FIP1L1/CHIC2/PDGFRA Deletion/Fusion



MPN **

Deletion of CHIC2 (*cysteine rich hydrophobic domain 2*) at 4q12 results in the fusion of FIP1L1 (*factor interacting with PAPOLA and CPSF1*) at 4q12 with PDGFRA (*platelet derived growth factor receptor alpha*) at 4q12 producing a tyrosine kinase which transforms haematopoietic cells[1].

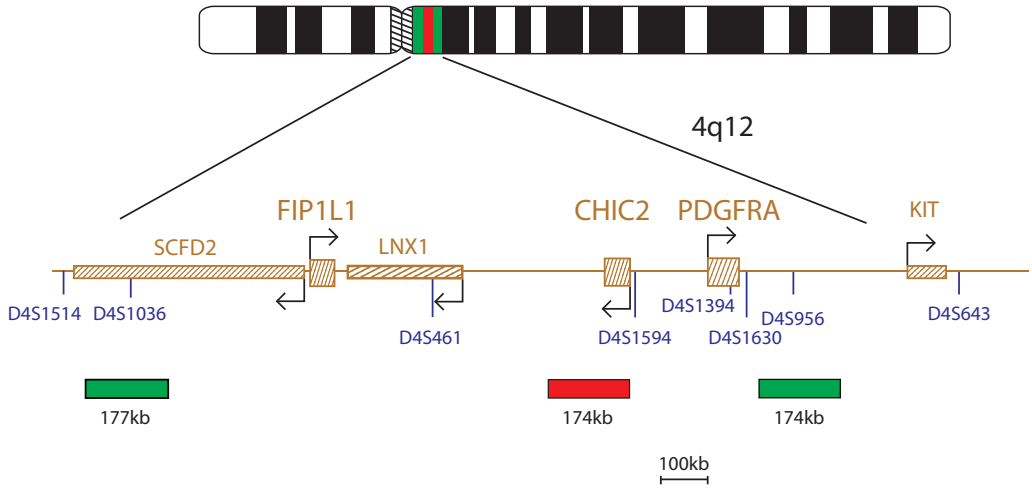
In the 2008 World Health Organization (WHO) classification of myeloid neoplasms and acute leukaemia, a new subgroup of myeloid neoplasms was introduced: *Myeloid and Lymphoid Neoplasms with Eosinophilia and Abnormalities of PDGFRA, PDGFRB or FGFR1*. These neoplasms constitute three specific disease groups, with some shared features[1].

The most common myeloproliferative neoplasms (MPN) showing PDGFRA rearrangements are those with FIP1L1-PDGFRA fusions. These MPNs present as chronic eosinophilic leukaemia (CEL) or, more rarely, as acute myeloid leukaemia (AML). As this abnormality is cytogenetically cryptic, FISH provides a useful tool for the detection of the fusion[1,2].

Patients with the fusion benefit from treatment with tyrosine kinase inhibitors (TKIs). The diagnosis of the fusion gene can therefore lead to therapeutic choices for the patient[1,2].

REFERENCES

1. Swerdlow *et al*., editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France, IARC:2008
2. Cools J *et al*., N Eng J Med 2003;348:1201-14



** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 014-S** (5 tests)
Cat. No. **LPH 014** (10 tests)

IGH Breakapart*

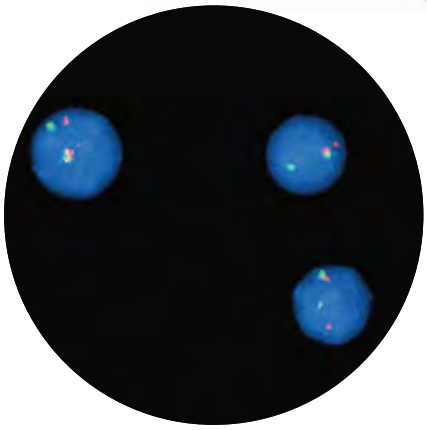
Recurrent rearrangements involving the IGH (*immunoglobulin heavy locus*) gene at 14q32.33 with a wide range of partner genes are seen in lymphomas and haematological malignancies[1].

A t(8;14)(q24;q32) translocation, involving IGH and the MYC gene at 8q24, is frequently seen in Burkitt lymphoma[2] and diffuse large B-cell lymphoma (DLBCL)[3]. Other rearrangements frequently reported in B-cell lymphoma include: the t(14;18)(q32;q21) translocation, involving IGH and the BCL2 gene, seen in both follicular lymphoma and DLBCL[4]; and the t(11;14)(q13;q32) involving IGH and the CCND1 gene, which is the hallmark of mantle cell lymphoma (MCL)[5].

IGH rearrangements with a number of different gene partners are a frequent finding in patients with multiple myeloma, including: t(4;14)(p16;q32) translocations involving IGH with FGFR3 and WHSC1; t(6;14)(p21;q32) translocations involving IGH and CCND3; t(11;14)(q13;q32) translocations involving IGH and CCND1; t(14;16)(q32;q23) translocations involving IGH and MAF, and t(14;20)(q32;q12) translocations involving IGH and MAFB[6,7].

IGH rearrangements are also reported as recurrent abnormalities in patients with lymphoplasmacytic lymphoma (LPL), chronic lymphocytic leukaemia (CLL), extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT) type and acute lymphoblastic leukaemia (ALL)[8].

The breakapart design for this probe set allows the detection of rearrangements of the IGH region, regardless of partner gene or chromosome involved.

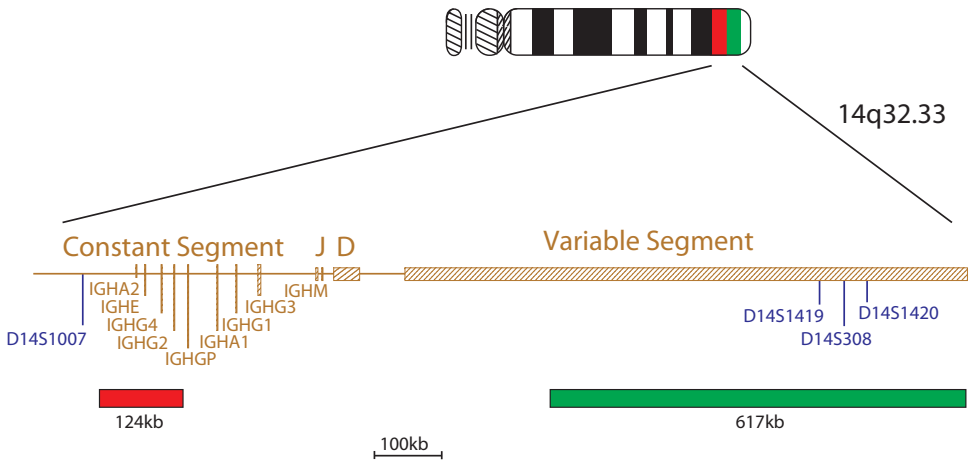


IGH-rearranged sample

ALL CLL L MM **

REFERENCES

1. Gozzetti A, *et al*. Cancer Res.2002 Oct 1;62(19):5523-7
2. Ferry JA. Oncologist 2006 Apr;11(4):375-83
3. Li S, *et al*. Mod Pathol. 2012 Jan;25(1):145-56
4. Snuderl M, *et al*. Am J Surg Pathol. 2010 Mar;34(3):327-40
5. Vose JM. Am J Hematol. 2013;88(12):1082-8
6. Bergsagel PL, *et al*. Proc Natl Acad Sci USA. 1996 Nov 26;93(24):13931-6
7. Sawyer JR. Cancer Genet. 2011 Jan;204(1):3-12
8. Swerdlow SH, *et al*, eds. 2008 WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC



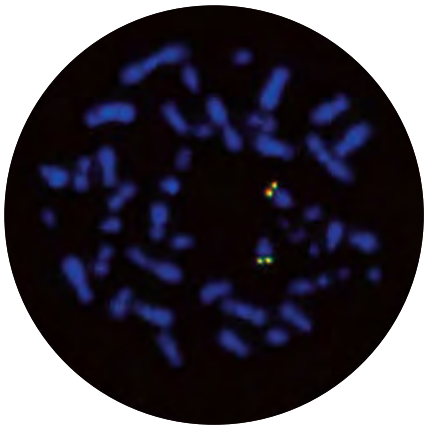
***A similar product is also available in the Haematopathology range, refer to page 86.**

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 070-S** (5 tests)
Cat. No. **LPH 070** (10 tests)

IGH *Plus* Breakapart*



ALL CLL L MM **

Recurrent rearrangements involving the IGH (*immunoglobulin heavy locus*) gene at 14q32.33 with a wide range of partner genes are seen in lymphomas and haematological malignancies[1].

A t(8;14)(q24;q32) translocation, involving IGH and the MYC gene at 8q24, is frequently seen in Burkitt lymphoma[2] and diffuse large B-cell lymphoma (DLBCL)[3]. Other rearrangements frequently reported in B-cell lymphoma include: the t(14;18)(q32;q21) translocation, involving IGH and the BCL2 gene, seen in both follicular lymphoma and DLBCL[4]; and the t(11;14)(q13;q32) involving IGH and the CCND1 gene, which is the hallmark of mantle cell lymphoma (MCL)[5].

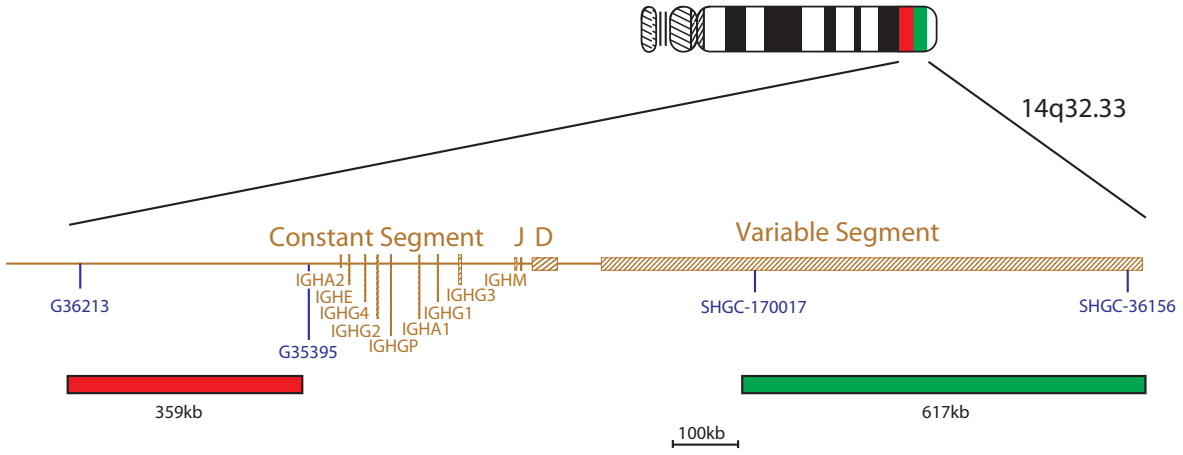
IGH rearrangements with a number of different gene partners are a frequent finding in patients with multiple myeloma, including: t(4;14)(p16;q32) translocations involving IGH with FGFR3 and WHSC1; t(6;14)(p21;q32) translocations involving IGH and CCND3; t(11;14)(q13;q32) translocations involving IGH and CCND1; t(14;16)(q32;q23) translocations involving IGH and MAF, and t(14;20)(q32;q12) translocations involving IGH and MAFB[6,7].

IGH rearrangements are also reported as recurrent abnormalities in patients with lymphoplasmacytic lymphoma (LPL), chronic lymphocytic leukaemia (CLL), extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT) type and acute lymphoblastic leukaemia (ALL)[8].

The breakapart design for this probe set allows the detection of rearrangements of the IGH region, regardless of partner gene or chromosome involved.

REFERENCES

1. Gozzetti A, *et al*. Cancer Res.2002 Oct 1;62(19):5523-7
2. Ferry JA. Oncologist 2006 Apr;11(4):375-83
3. Li S, *et al*. Mod Pathol. 2012 Jan;25(1):145-56
4. Snuderl M, *et al*. Am J Surg Pathol. 2010 Mar;34(3):327-40
5. Vose JM. Am J Hematol. 2013;88(12):1082-8
6. Bergsagel PL, *et al*. Proc Natl Acad Sci USA. 1996 Nov 26;93(24):13931-6
7. Sawyer JR. Cancer Genet. 2011 Jan;204(1):3-12
8. Swerdlow SH, *et al*, eds. 2008 WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC



*** A similar product is also available within the Haematopathology range, refer to page 86.**

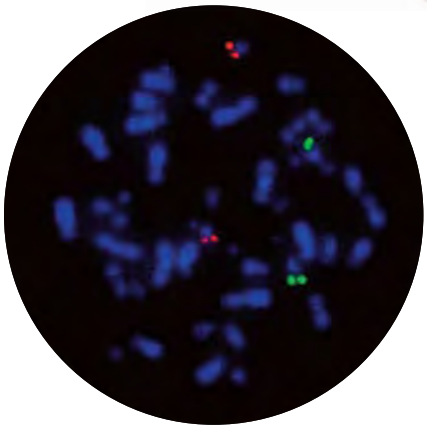
** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 071-S** (5 tests)

Cat. No. **LPH 071** (10 tests)

IGH/BCL2 *Plus* Translocation, Dual Fusion*



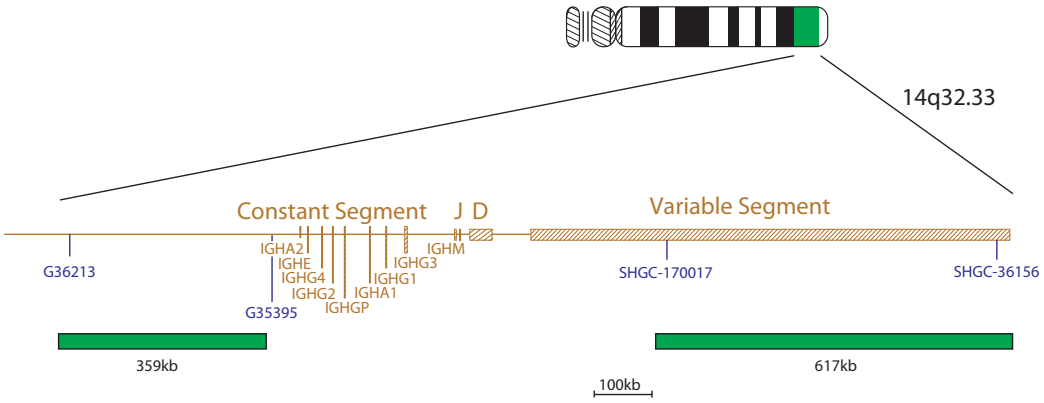
CLL L **

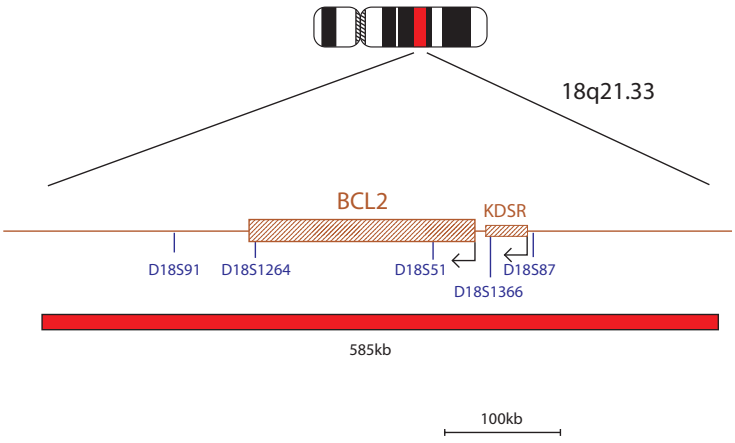
The t(14;18)(q32;q21) translocation involving the IGH (*immunoglobulin heavy locus*) gene at 14q32.33 and the BCL2 (*B-cell CLL/ lymphoma 2*) gene at 18q21.33 is a recognised recurrent abnormality seen in B-cell malignancies.

IGH-BCL2 rearrangements are observed in 70-95% of follicular lymphoma (FL) cases and 20-30% of diffuse large B-cell lymphoma (DLBCL)[1]. Presence of the t(14;18) translocation in DLBCL is a predictor of outcome and has a poor prognostic effect[2]. BCL2 translocations have also been implicated in chronic B-cell lymphoproliferative disease (CLPD) and also occur occasionally in chronic lymphocytic leukaemia (CLL)[3].

REFERENCES

1. Tomita N., J Clin Exp Hematop 2011;51(1):7-12
2. Barrans *et al*., Clin Cancer Res 2003; 9; 2133
3. Bassegio L *et al*., Br J Haematol 2012;158(4):489-98





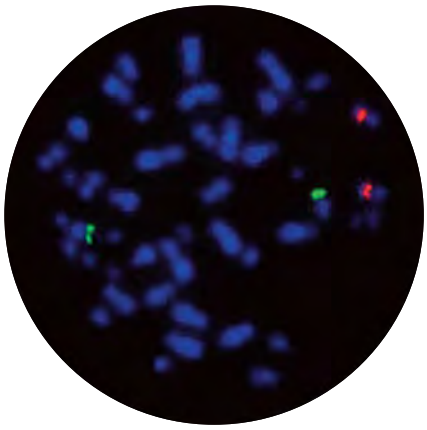
*** A similar product is also available within the Haematopathology range, refer to page 87.**

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 072-S** (5 tests)
Cat. No. **LPH 072** (10 tests)

IGH/CCND1 *Plus* Translocation, Dual Fusion*



L **

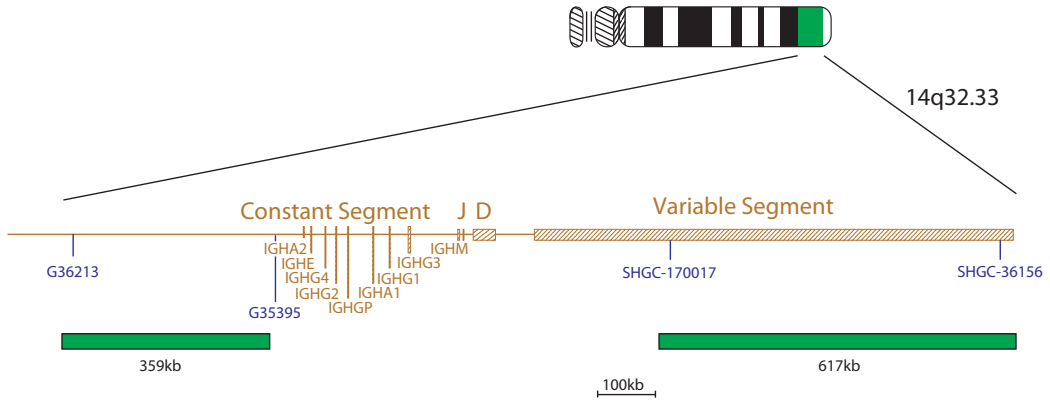
The t(11;14)(q13;q32) translocation involving CCND1 (*cyclin D1*) gene at 11q13.3 and the IGH (*immunoglobulin heavy locus*) gene at 14q32.33 is associated with mantle cell lymphoma.

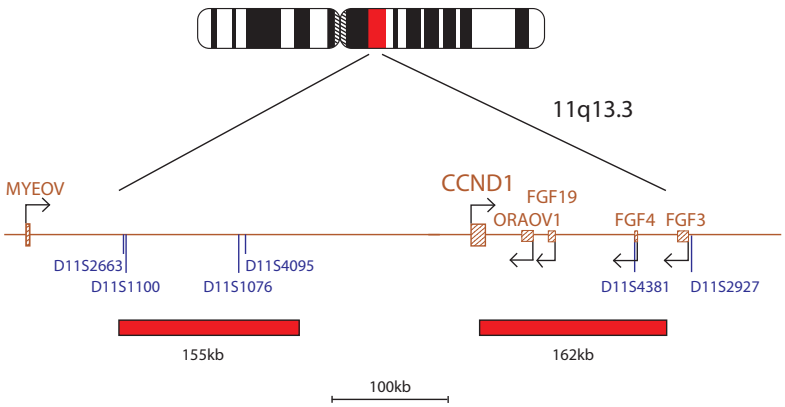
The t(11;14)(q13;q32) rearrangement involving CCND1 and IGH is considered the hallmark of mantle cell lymphoma (MCL)[1], the presence of which can be used to aid in the differential diagnosis of CD5+ B-cell lymphoproliferative disorders[2].

Amplification of the CCND1 region has been reported in a number of solid tumours including breast cancer[3], squamous cell carcinoma[4] and gastric cancer[5].

REFERENCES

1. Vose JM. Am J Hematol. 2013;88(12):1082-8
2. Ho AK, *et al*. Am J Clin Pathol 2009;131:27-32
3. Roy PG *et al*. Int J Cancer [Internet] 2010;127:355-60
4. Mahdey HM, *et al*. Asian Pac J Cancer Prev 2011;12:2199-204
5. Stahl P, *et al*. BMC Gastroenterol 2015;15:7





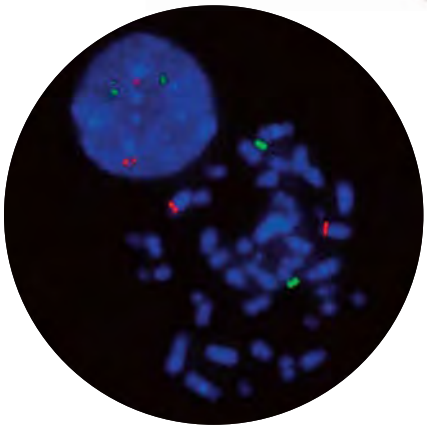
*** A similar product is also available within the Haematopathology range, refer to page 88.**

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 075-S** (5 tests)
Cat. No. **LPH 075** (10 tests)

IGH/CCND3 *Plus* Translocation, Dual Fusion



L MM **

The CCND3 (*cyclin D3*) gene is located at 6p21.1 and IGH (*immunoglobulin heavy locus*) at 14q32.33.

Approximately 50-60% of multiple myeloma (MM) cases are associated with translocations involving IGH and one of several partners including CCND1, WHSC1 (MMSET) and FGFR3, CCND3, MAF or MAFB[1].

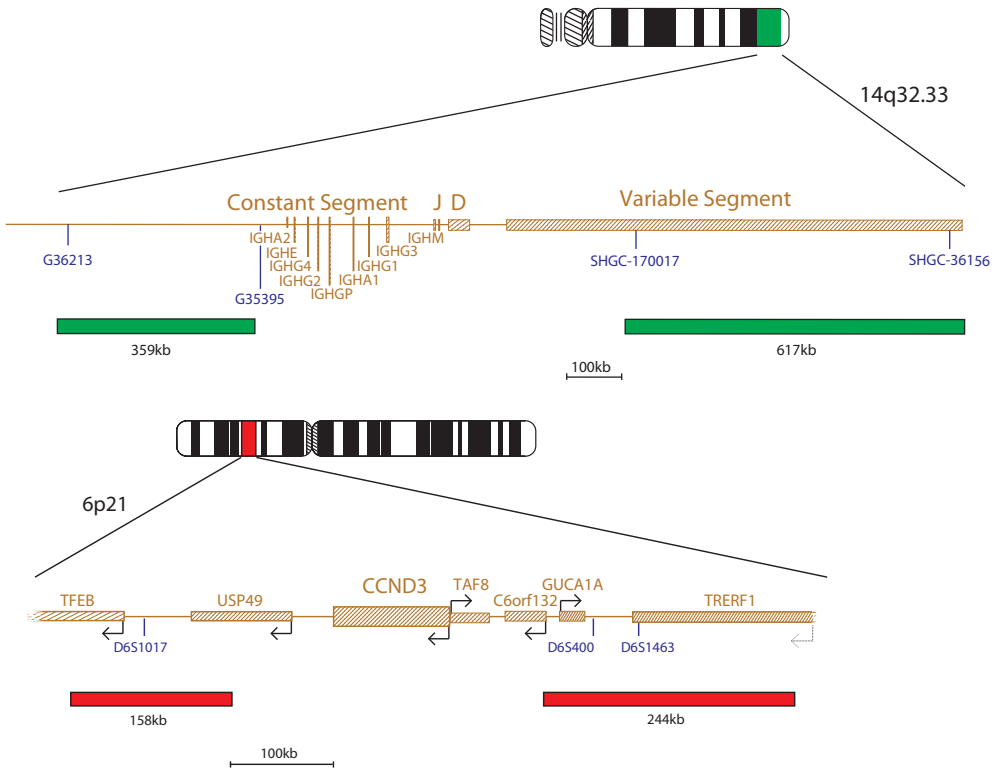
The t(6;14)(p21;q32) translocation is a recurrent translocation seen in 4% of cases of MM[2].

CCND3 has been identified as a putative oncogene that is dysregulated as a consequence of the t(6;14)(p21;q32) translocation[2]. The translocation appears to be mediated by an error in IgH switch recombination as it has been shown that in KMM-1 cell lines, the translocation disrupts a switch sequence in this region and results in juxtaposition of CCND3 with the IGH promoter, thus elevating the levels of CCND3 expression[2]. It is thought that this mechanism is similar in all cases of IGH translocation. Most breakpoints appear to be clustered in a region that is fewer than 200kb centromeric to CCND3[2].

CCND3-IGH translocations are also reported in a variety of other B-cell malignancies, including plasma cell leukaemia, diffuse large B-cell lymphoma (DLBCL) and splenic lymphoma with villous lymphocytes (SLVL)[3].

REFERENCES

1. Fonseca et al., Cancer Res 2004;64:1546-58
2. Shaughnessy et al., Blood 2001;98(1):217-23
3. Soniki et al., Blood 2001;98(9):2837-44

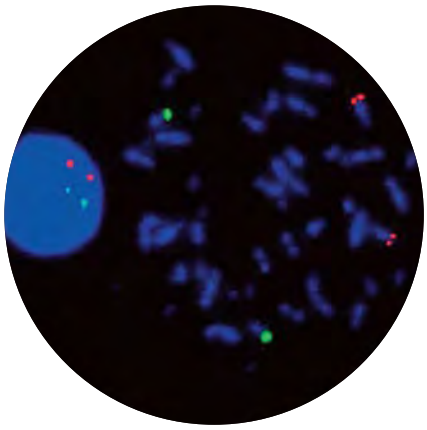


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 076-S** (5 tests)
Cat. No. **LPH 076** (10 tests)

IGH/cMYC (MYC) *Plus* Translocation, Dual Fusion*



L **

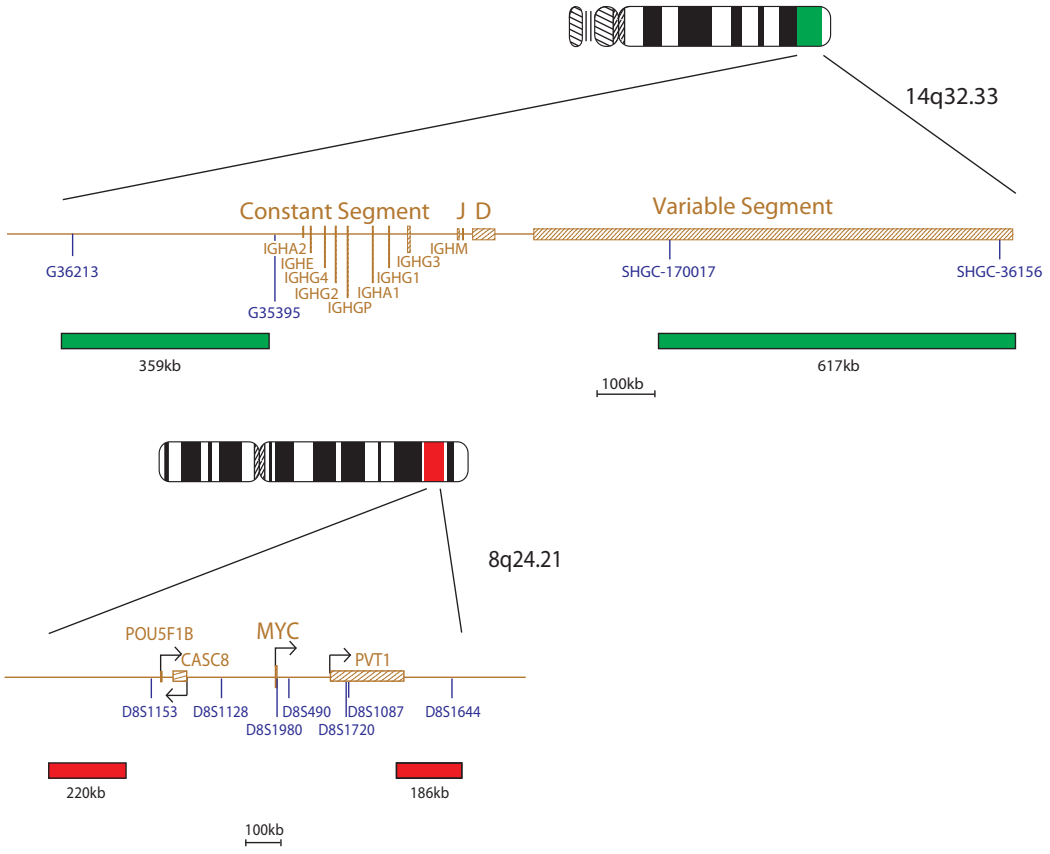
The t(8;14)(q24;q32) translocation involving the IGH (*immunoglobulin heavy locus*) gene at 14q32.33 and the MYC (*v-myc avian myelocytomatosis viral oncogene homolog*) oncogene at 8q24 is a recognised recurrent abnormality commonly seen in patients with B-cell malignancy.

IGH-MYC rearrangements are detected in up to 85% of cases of Burkitt lymphoma at diagnosis[1]. They are also seen in diffuse large B-cell lymphoma (DLBCL)[2], multiple myeloma and plasmablastic lymphoma[3,4].

In an IGH-MYC rearrangement the translocation breakpoints on chromosome 14 are clustered to a narrow region 5' to the intron enhancer of the immunoglobulin heavy chain, whereas the breakpoints on chromosome 8 can occur more than 340kb upstream of MYC, with no preferential site[5]. The translocation brings MYC into close proximity to the IGH enhancer and results in the up-regulation of MYC. Over-expression of the transcription factor stimulates gene amplification, resulting in uncontrolled cell proliferation[6].

REFERENCES

1. Perkins AS, Friedberg JW. Hematology Am Soc Hematol Educ Program. 2008;341-8
2. Ott G, *et al*. Blood. 2013 Dec 5;122(24):3884-91
3. Walker BA, *et al*. Blood Cancer J. 2014;4(3)
4. Elyamany G, *et al*. Adv Hematol 2015;2015:315289
5. Joos *et al*., Human Molecular Genetics 1992;1(8):625-32
6. Erikson J *et al*., Proc Natl Acad Sci USA 1983;80(3):820-4



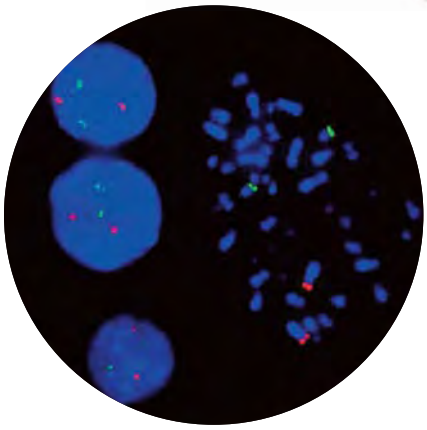
*** A similar product is also available within the Haematopathology range, refer to page 90.**

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 074-S** (5 tests)
Cat. No. **LPH 074** (10 tests)

IGH/FGFR3 *Plus* Translocation, Dual Fusion



MM **

The FGFR3 (*fibroblast growth factor receptor 3*) gene is located at 4p16.3 and IGH (*immunoglobulin heavy locus*) at 14q32.33.

Approximately 50-60% of multiple myeloma (MM) cases are associated with translocations involving IGH and one of several partners including CCND1, WHSC1 (MMSET) and FGFR3, CCND3, MAF or MAFB[1].

The t(4;14)(p16;q32) translocation is a recurrent translocation seen in 15% of MMs[2,3].

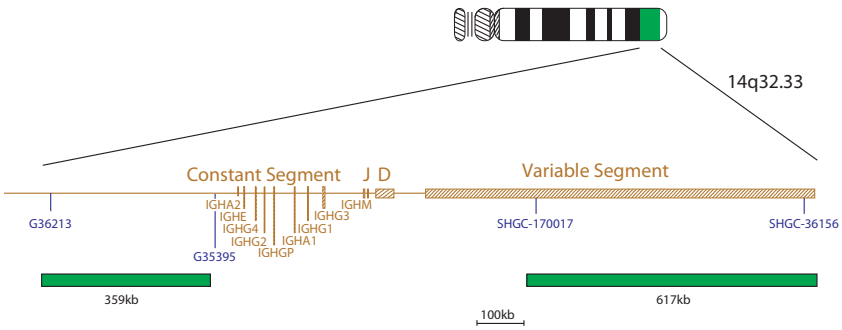
The translocation results in the dysregulation of two genes at 4p16; WHSC1 (*Wolf-Hirschhorn syndrome candidate 1*) and FGFR3. The consequence of the translocation is increased expression of FGFR3 and WHSC1. The translocation can be unbalanced, with 25% of cases losing the derivative chromosome 14, associated with the loss of FGFR3 expression[2,3].

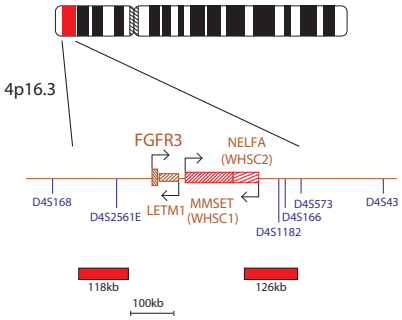
The majority of the breakpoints on chromosome 4 occur between FGFR3 and WHSC1. The breakpoint on chromosome 14 is almost exclusively in the switch region of constant genes. For the overexpression of both FGFR3 and WHSC1 the breakpoint on chromosome 14 must be located between the μ enhancer and the 3' IGH enhancers and between FGFR3 and WHSC1. As a consequence both derivative chromosomes contain an enhancer juxtaposed to an oncogene[4].

This t(4;14) translocation is often cytogenetically cryptic and was poorly described before the advent of FISH techniques. The translocation has been associated with poorer survival in MM patients[2,3].

REFERENCES

1. Fonseca *et al*., Cancer Res 2004;64:1546-58
2. Fonseca *et al*., Leukemia 2009;23(12):2210-2221
3. Sawyer, Cancer Genetics 2011;204(1):3-12
4. Walker *et al*., Blood 2013;121(17);3413-3419



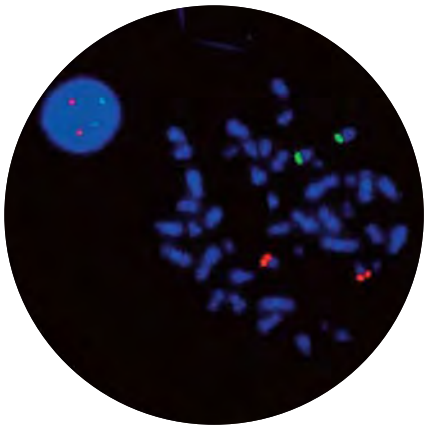


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 073-S** (5 tests)
Cat. No. **LPH 073** (10 tests)

IGH/MAF *Plus* Translocation, Dual Fusion



MM **

MAF (*v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog*) gene is located at 16q23.2 and IGH (*immunoglobulin heavy locus*) at 14q32.33.

Approximately 50-60% of multiple myeloma (MM) cases are associated with translocations involving IGH and one of several partners including CCND1, WHSC1 (MMSET) and FGFR3, CCND3, MAF or MAFB[1].

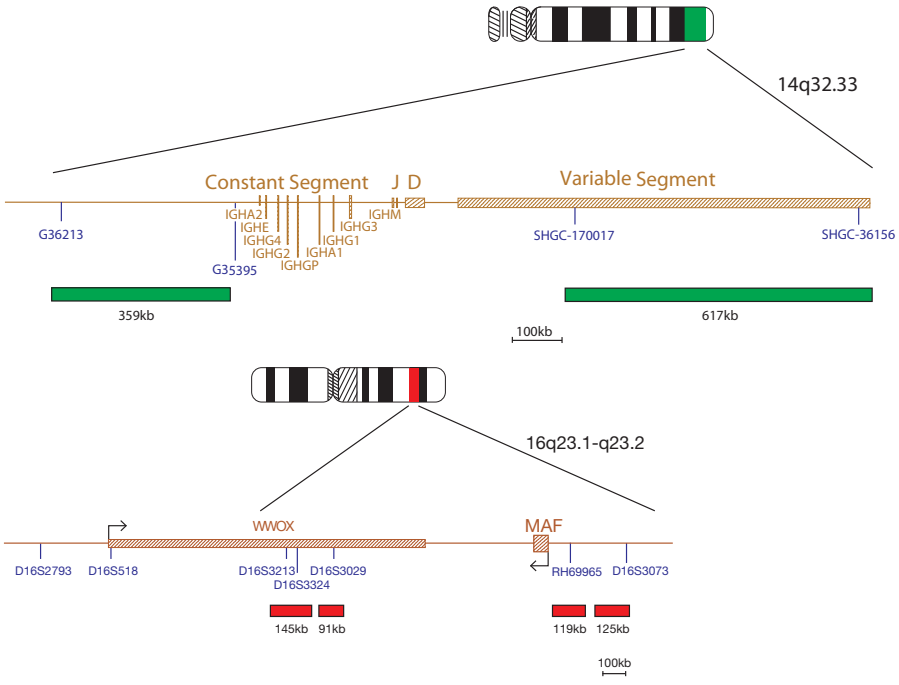
The t(14;16)(q32;q23) translocation is a recurrent translocation seen in 5% of MMs[1].

The majority of the breakpoints occur within the last intron of WWOX (*WW domain containing oxidoreductase*), centromeric to MAF. These breakpoints have a dual impact of positioning the IGH enhancer near MAF and disrupting the WWOX gene[2]. Gene expression profiling of myeloma cell lines revealed that MAF caused transactivation of cyclin D2 (a promoter of cell cycle progression), thus enhancing proliferation of myeloma cells[3]. The putative tumour suppressor gene, WWOX, spans the common chromosomal fragile site 16D (FRA16D) at chromosome 16q23-24 – a region that is a frequent target for both loss of heterozygosity and chromosomal rearrangements in ovarian, breast, lung, hepatocellular and prostate carcinomas as well as other neoplasias[4].

MM patients harbouring the t(14;16) appear to have a more aggressive clinical outcome[5,6].

REFERENCES

1. Fonseca *et al*., Cancer Res 2004;64:1546-1558
2. Walker *et al*., Blood 2013;121(17);3413-3419
3. Chang H *et al*., Leukemia 2007;21:1572-1574
4. Nunez MI *et al*., BMC Cancer 2005;5:64
5. Fonseca *et al*., Leukemia 2009;23(12):2210-2221
6. Sawyer, Cancer Genetics 2011;204(1):3-12

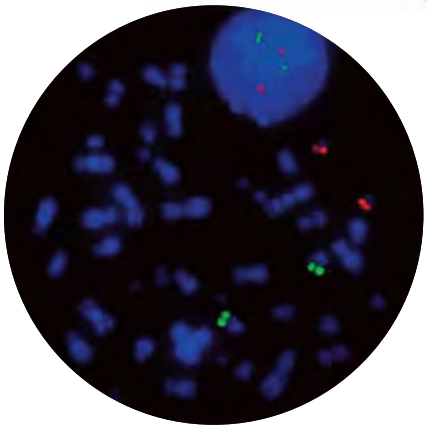


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 077-S** (5 tests)
Cat. No. **LPH 077** (10 tests)

IGH/MAFB *Plus* Translocation, Dual Fusion



MM **

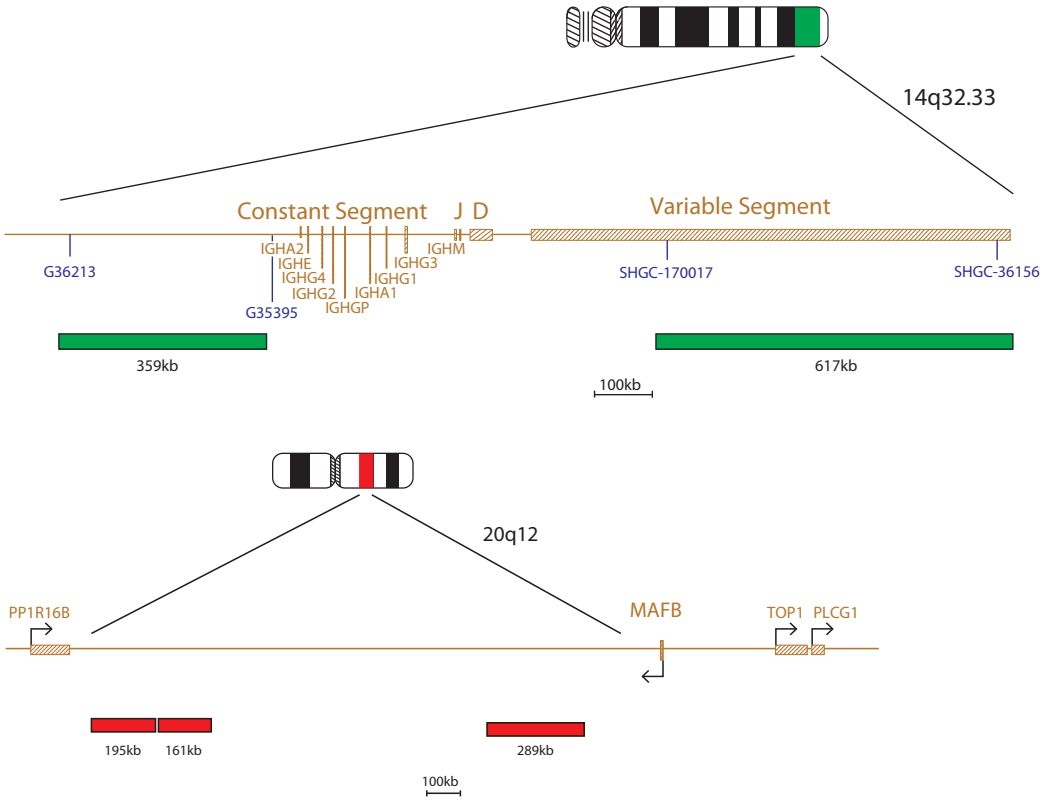
The MAFB (*v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog B*) gene is located at 20q12 and IGH (*immunoglobulin heavy locus*) at 14q32.33.

Approximately 50-60% of multiple myeloma (MM) cases are associated with translocations involving IGH and one of several partners including CCND1, WHSC1 (MMSET) and FGFR3, CCND3, MAF or MAFB[1].

The t(14;20)(14q32;q12) translocation is a recurrent translocation seen in around 2% of MMs[2,3].

The reciprocal rearrangement brings a truncated form of the IGH µ-enhancer (Eµ, located between the joining (J) segments and the constant region of the IGH gene) in close contact with the MAFB gene[4]. The resultant fusion and the up-regulated transcription product has been shown to cause dysregulation of cyclin D2[1].

The prognostic outcome of t(14;20)(14q32;q12) is assumed to be the same as the t(14;16)(q32;q23)[3].



REFERENCES

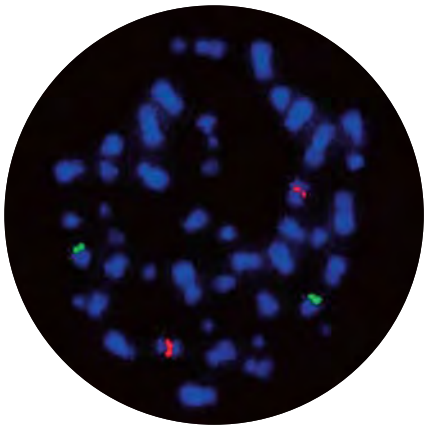
1. Fonseca *et al*., Cancer Research 2004;64:1546-1558
2. Fonseca *et al*., Leukemia 2009;23(12):2210-2221
3. Sawyer, Cancer Genetics 2011;204(1):3-12
4. Boersma-Vreugdenhil *et al*., Br J Haematol 2004;126:355-63

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 078-S** (5 tests)
Cat. No. **LPH 078** (10 tests)

IGH/MYEOV *Plus* Translocation, Dual Fusion



MM **

The MYEOV (*myeloma overexpressed*) gene is located at 11q13.3 and IGH (*immunoglobulin heavy locus*) at 14q32.33.

Approximately 50-60% of multiple myeloma (MM) cases are associated with translocations involving IGH and one of several partners including CCND1, WHSC1 (MMSET) and FGFR3, CCND3, MAF or MAFB[1].

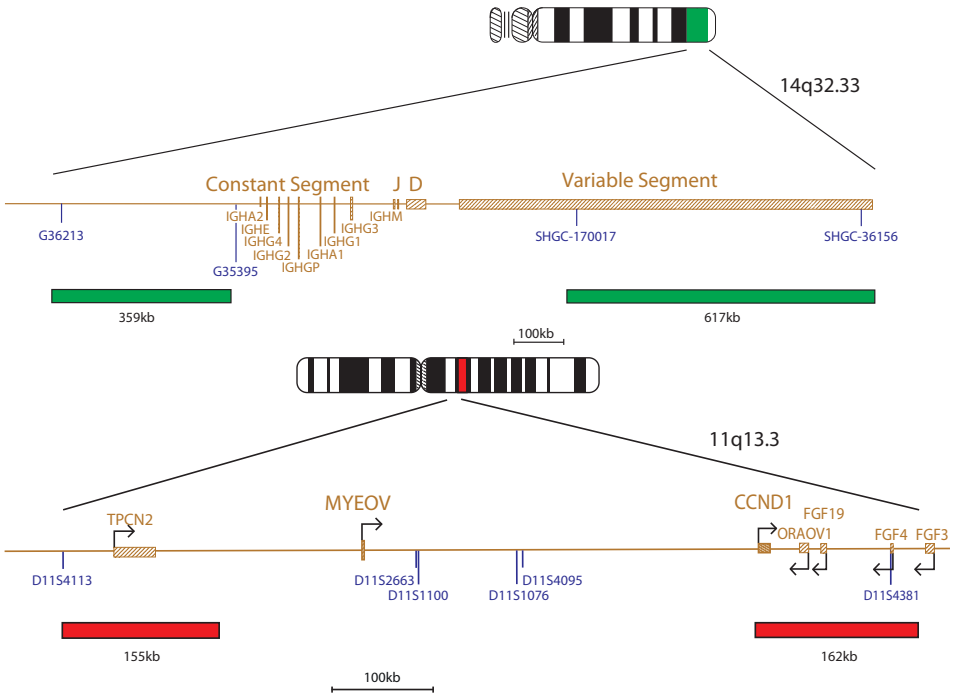
The t(11;14)(q13;q32) translocation is the most common translocation in MM, where it is seen in approximately 15% of cases [2,3].

Unlike mantle cell lymphoma (MCL), where the breakpoints are clustered in a 1kb region that is 120kb centromeric to the CCND1 gene[4], the breakpoints in MM cases are dispersed within a 360kb region between CCND1 and MYEOV at 11q13[5]. MYEOV is a putative oncogene, located 360kb centromeric to CCND1, which is thought to be activated in the translocation by becoming closely associated with IGH enhancers. In contrast to IGH rearrangements in other neoplasms, those found in MM have IGH breakpoints predominantly in the C/J region, which, in the case of MYEOV, brings the MYEOV gene under the control of the 3' Eα1 enhancer[5]. In CCND1 translocations by contrast, the Eμ enhancer controls CCND1 expression. MYEOV overexpression is a possible prognostic factor in MM[6].

The t(11;14)(q13;q32) is associated with a favourable outcome in most series and therefore is regarded as neutral with regard to prognosis[3].

REFERENCES

1. Fonseca *et al*., Cancer Res 2004;64:1546-1558
2. Fonseca *et al*., Leukemia 2009;23(12):2210-2221
3. Sawyer, Cancer Genetics 2011;204(1):3-12
4. Ronchetti *et al*., Blood 1999 93(4):1330-1337
5. Janssen *et al*., Blood. 2000 15;95(8):2691-2698
6. Moreaux *et al*., Exp Haematol 2010;38(12):1189-1198



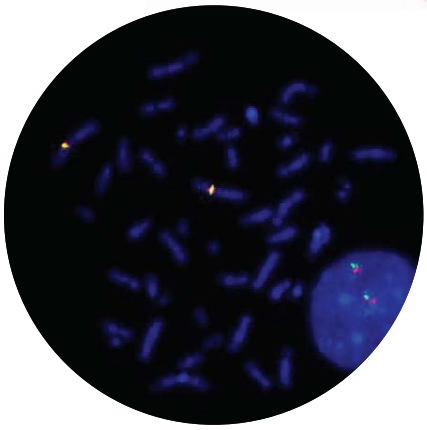
** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

IGK Breakapart and IGL Breakapart*

Recurrent rearrangements involving the IGK (*immunoglobulin kappa locus*) gene at 2p11.2 or the IGL (*immunoglobulin lambda locus*) gene at 22q11, with a wide range of partner genes, are seen in lymphomas and haematological malignancies.

A large number of B-cell malignancies harbour translocations involving the immunoglobulin (IG) loci. The majority of cases will show rearrangements involving the IGH gene; however, variant translocations have been described in 5-10% of B-cell neoplasms which involve either the immunoglobulin kappa (IGK) light chain locus at 2p11.2 or the immunoglobulin lambda (IGL) light chain locus at 22q11[1,2].

Variant translocations involving the IG light chain loci are seen in Burkitt lymphoma and multiple myeloma, with the presence of a t(2;8)(p12;q24) MYC-IGK, or t(8;22)(q24;q11) MYC-IGL[3,5]. In diffuse large B-cell lymphoma (DLBCL), translocations may involve the BCL6 gene via t(2;3)(p12;q27) or t(3;22)(q27;q11) translocations, or the BCL2 gene via t(2;18)(p12;q21) or t(18;22)(q21;q11) translocations[6].



IGK Breakapart

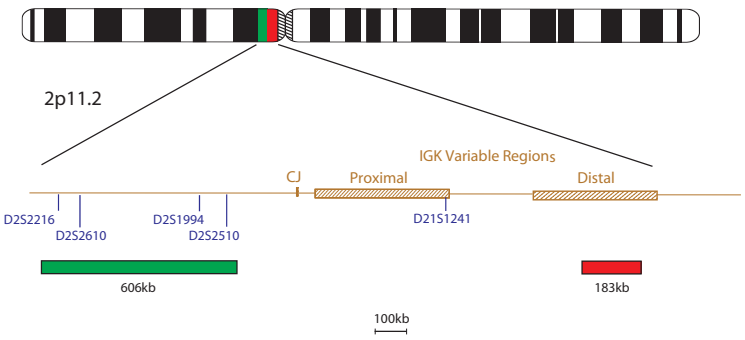
L **

IGL Breakapart

L **

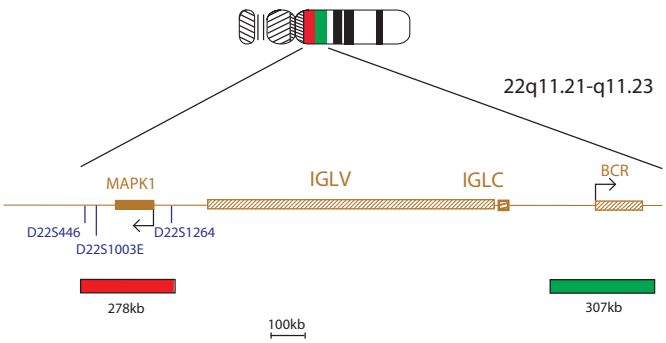
IGK Breakapart

Cat. No. **LPH 034**



IGL Breakapart

Cat. No. **LPH 033**



REFERENCES

1. Poulseu TS *et al*., Leukemia 2002;16:2148-55
2. Martin-Subero JI *et al*., Int J Cancer 2002;98:470-4
3. Kornblau SM *et al*., Hematol Oncol 1991;9:63-78
4. Walker BA, *et al*. Blood Cancer J; 2014;4(3):e191
5. Chaganti SR *et al*., Genes Chromosomes Cancer 1998;23:323-7
6. Tashiro S *et al*., Oncogene 1992;7:573-7

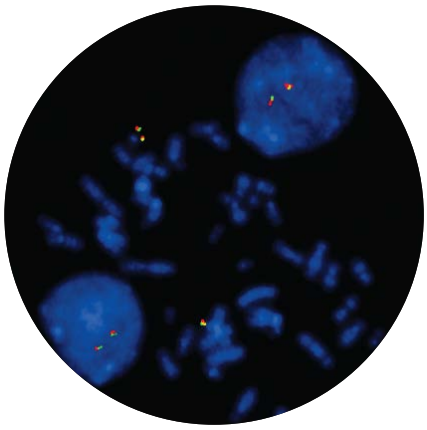
*** Similar products are also available within the Haematopathology range, refer to page 91**

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 013-S** (5 tests)
Cat. No. **LPH 013** (10 tests)

MLL (KMT2A) Breakapart



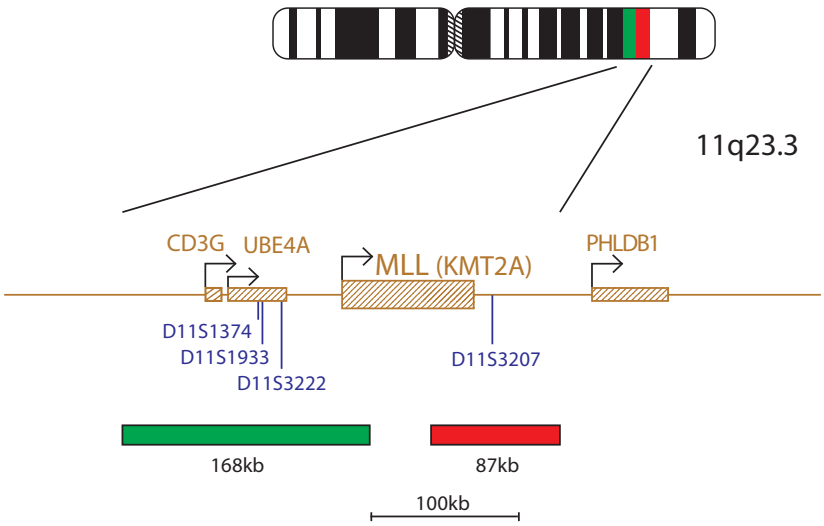
ALL AML **

The KMT2A *(lysine (K)-specific methyltransferase 2A)* gene at 11q23.3 is commonly rearranged in acute leukaemias, especially in infant leukaemia and in secondary leukaemia, following treatment with DNA topoisomerase II inhibitors[1].

The KMT2A gene has a great homology with the drosophila trithorax gene and encodes for a histone methyltransferase, which functions as an epigenetic regulator of transcription. KMT2A translocations result in the production of a chimeric protein in which the amino-terminal portion of KMT2A is fused to the carboxy-terminal portion of the fusion partner gene. The functional protein plays a critical role in embryonic development and haematopoiesis[1,2,3,4].

KMT2A rearrangements can be detected in approximately 80% of infants with acute lymphoblastic leukaemia (ALL) and in 5-10% of paediatric and adult ALLs[3,4]. They can also be found in 60% of infant acute myeloid leukaemia (AML) and in 3% of *de novo* and 10% of therapy related adult AML cases[3,5]. To date, more than 70 partners have been identified with the most common translocations being MLL-AFF1; t(4;11)(q21;q23.3), MLL-MLLT4; t(6;11)(q27;q23.3), MLL-MLLT3; t(9;11)(p22;q23.3) and MLL-MLLT1; t(11;19)(q23.3;p13.3)[1].

Historically, KMT2A rearrangements in acute leukaemia were associated with a poorer outcome, but recent studies have shown that the prognosis is highly dependent on the fusion partner and it may differ between children and adults[1].

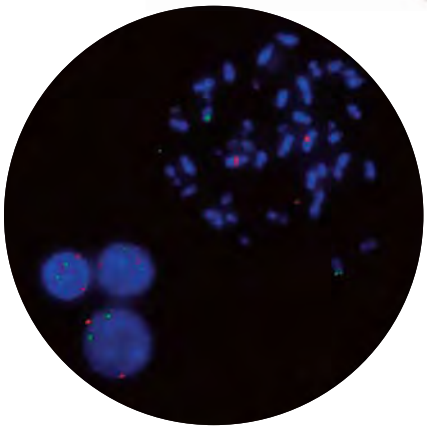


REFERENCES

1. Tamai, Inokuchi, J Clin Exp Hematopathol 2010;50(2):91-98
2. Wright, Vaughan, Critical Reviews in Oncology/Hematology 2014;91(3):283-291
3. Van der Burg *et al*., Leukemia 2004;18(5):895-908
4. Tomizawa, Pediatr Int 2015;57(8):811-819
5. Grossman *et al*., Leukemia 28 March 2013; doi10.1038/leu.2013.90

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

MLL (KMT2A)/AFF1 Translocation, Dual Fusion



ALL AML **

The KMT2A (*lysine (K)-specific methyltransferase 2A*) gene located at 11q23.3 and AFF1 (*AF4, AF4/FMR2 family member 1*) gene at 4q21.3 are involved in translocation t(4;11)(q21;q23.3), the most frequently observed translocation involving the KMT2A gene, in acute lymphoblastic leukaemia (ALL)[1].

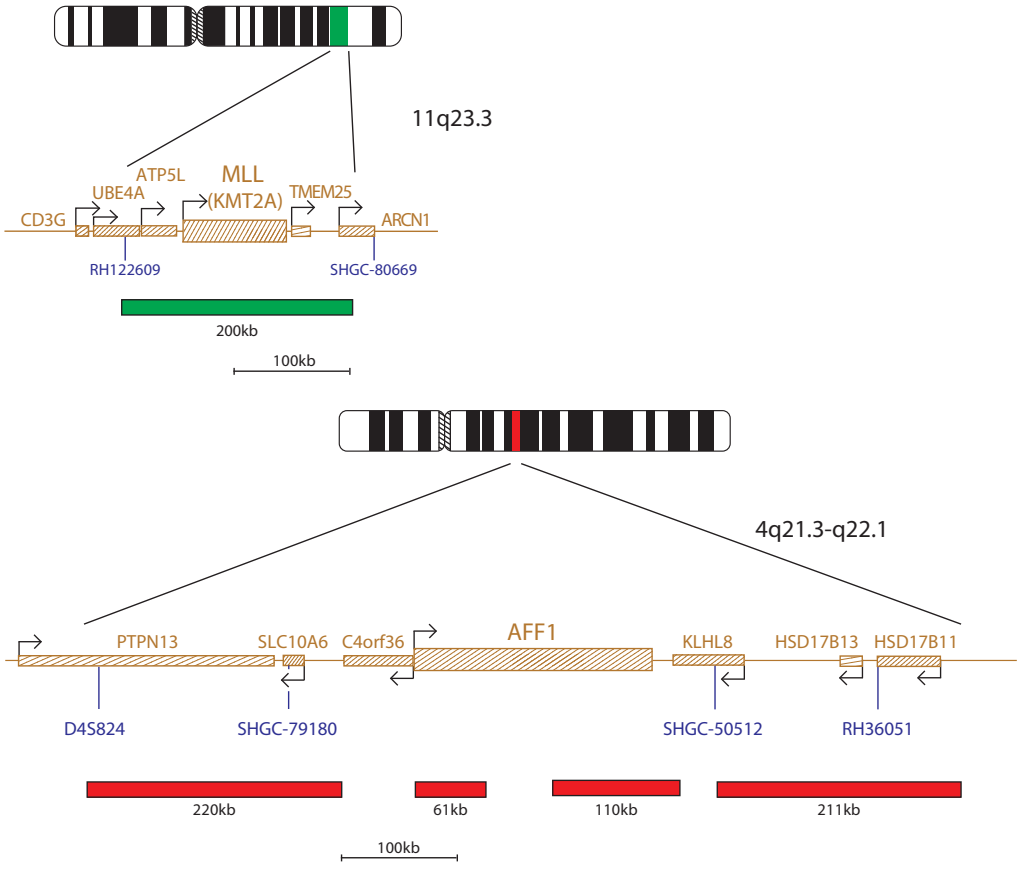
The t(4:11)(q21;q23.3) translocation results in the generation of two reciprocal fusion genes: KMT2A-AFF1 and AFF1-KMT2A – the leukaemic properties of the first have been documented but the role of the AFF1-KMT2A fusion protein is still under debate[2,3,4].

UK best practice guidelines suggest that, if chromosome analysis is unsuccessful but FISH indicates a rearrangement of KMT2A, then further attempts to identify the t(4;11) must be made as the t(4;11)(q21;q23) is associated with a poor prognosis, and patients with this translocation may be treated on the high risk arm of MRC protocols[5].

The MLL/AFF1 translocation, dual fusion probe allows both fusion genes, generated by the t(4;11)(q21;q23) translocation, to be detected.

REFERENCES

1. Meyer et al., Leukemia 2009;23(8):1490-9
2. Smith et al., Genes Dev. 2011;25(7): 661-72
3. Kumar et al., Leuk Res. 2011;35(3):305-9
4. Bursen et al., Blood. 2010; 29;115(17):3570-9
5. Professional Guidelines for Clinical Cytogenetics: Acute Lymphoblastic Leukaemia Best Practice Guidelines (2011) V1.00. www.cytogenetics.org.uk



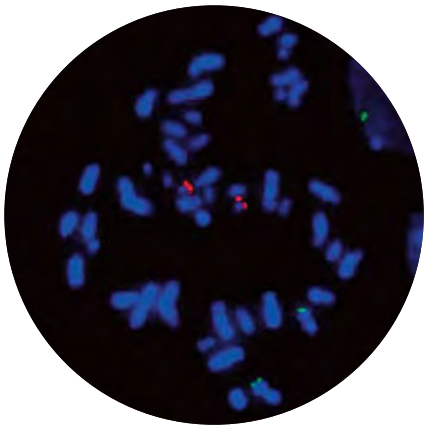
** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **RU-LPH 082-S†** (50µl)

Cat. No. **RU-LPH 082†** (100µl)

MLL/MLLT1†, MLL/MLLT3† and MLL/MLLT4† Translocation, Dual Fusion



MLL/MLLT1 Translocation, Dual Fusion

ALL AML **

Translocations involving KMT2A (*lysine (K)-specific methyl-transferase 2A*) at 11q23.3 frequently occur in both acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL).

The most common KMT2A rearrangement in both AML and ALL involves fusion of the KMT2A and AFF1 genes via a t(4;11)(q21;q23) translocation. Three of the other more common translocations involve the MLLT3 gene on chromosome 9, the MLLT1 gene on chromosome 19 or the MLLT4 gene on chromosome 6.

- KMT2A-MLLT3 - t(9;11)(p22;q23.3)
- KMT2A-MLLT1 - t(11;19)(q23.3;p13.3)
- KMT2A-MLLT4 - t(6;11)(q27;q23.3)

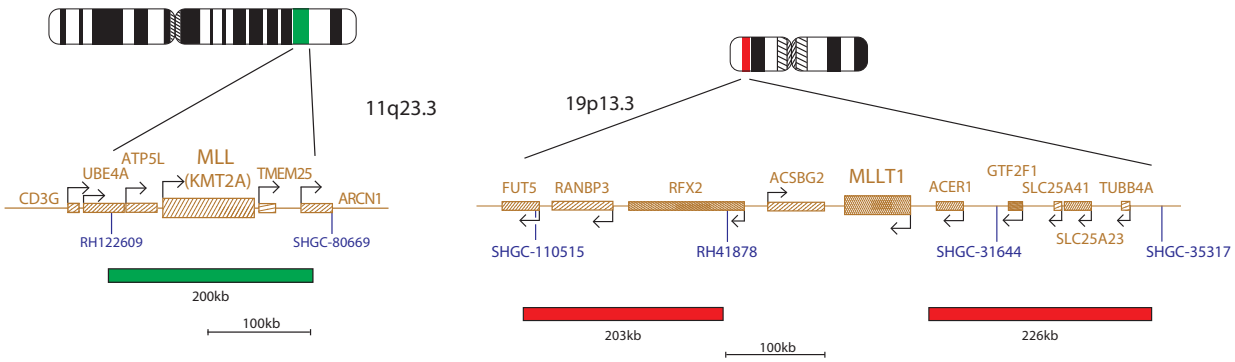
These Research Use Only (RUO) probe sets have been designed to allow the detection of these three recurrent KMT2A rearrangements.

REFERENCES

- Meyer *et al.,* Leukemia 2013;27(11):2165-76

MLL/MLLT1

Cat. No. **RU-LPH 082†**

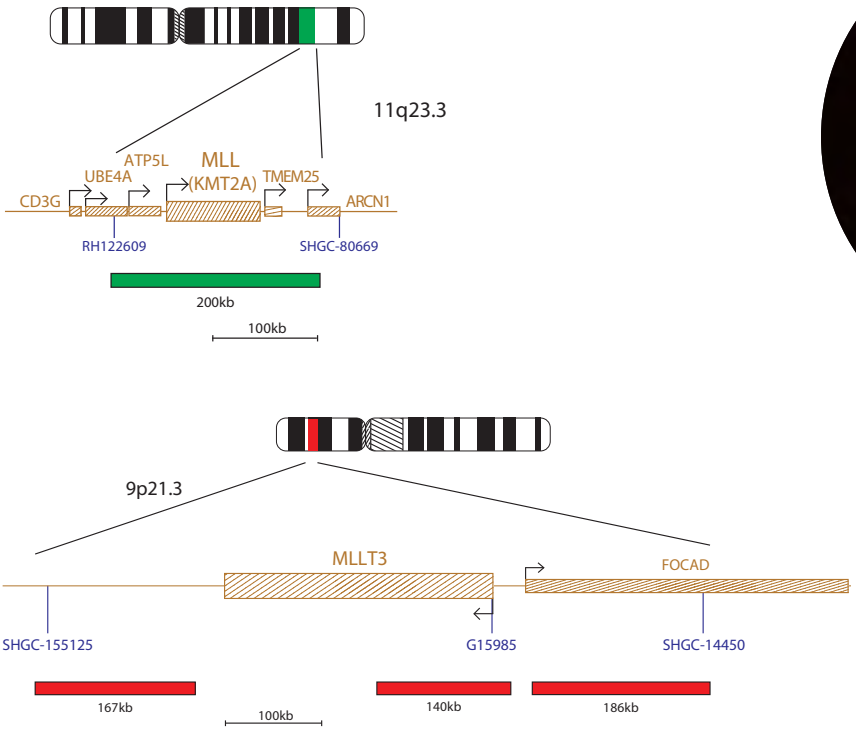


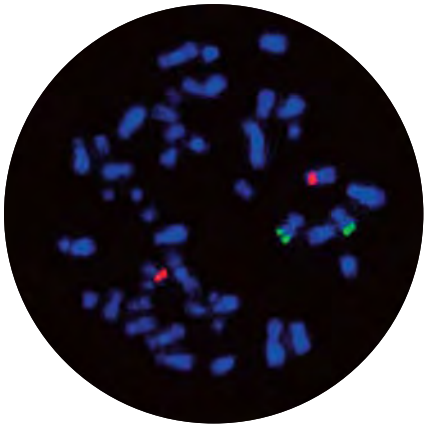
† For research use only, not for use in diagnostic procedures.

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

MLL/MLLT3

Cat. No. **RU-LPH 083†**

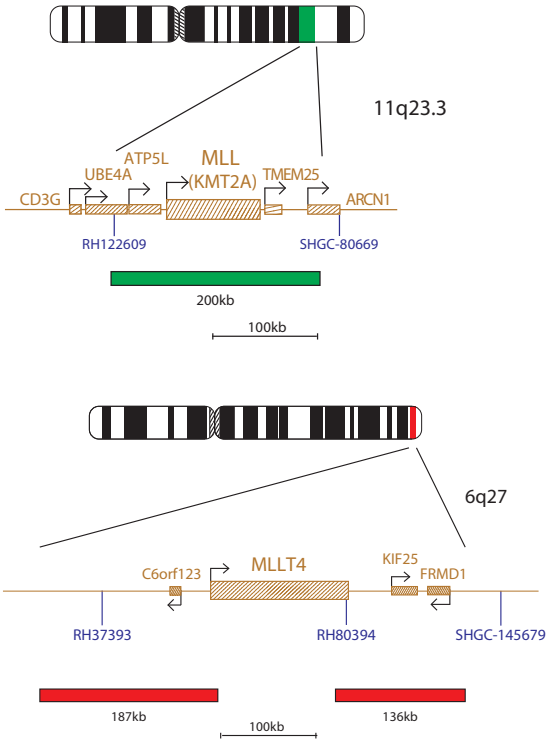


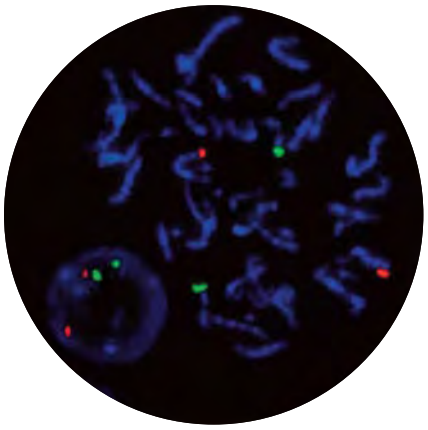


MLL/MLLT3 Translocation/Dual Fusion

MLL/MLLT4

Cat. No. **RU-LPH 084†**





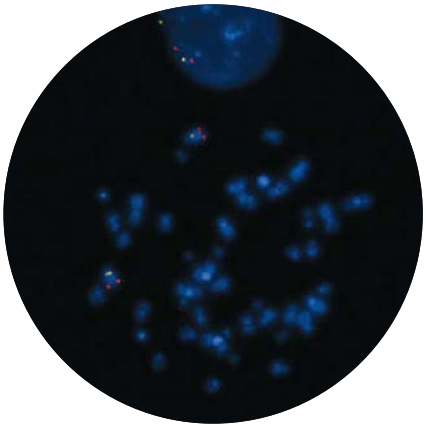
MLL/MLLT4 Translocation/Dual Fusion

†For research use only, not for use in diagnostic procedures.

Cytocell an OGT company aquarius

Cat. No. **LPH 016-S** (5 tests)
Cat. No. **LPH 016** (10 tests)

MYB Deletion

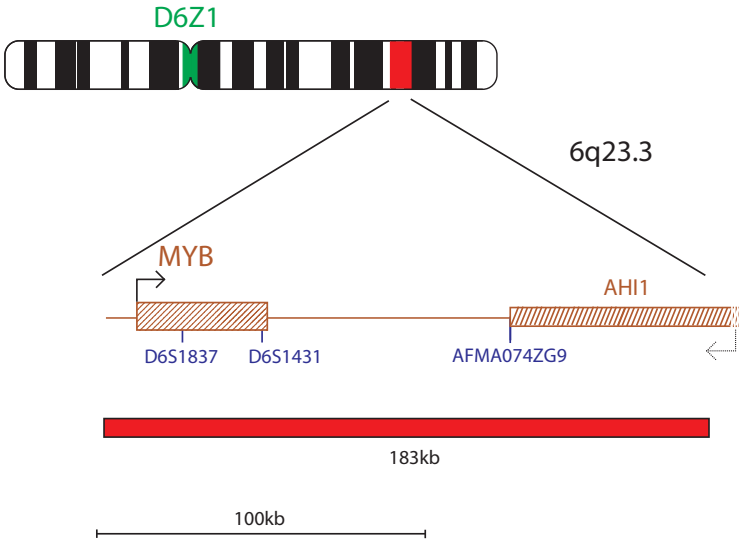


ALL CLL L **

MYB (*v-myb avian myeloblastosis viral oncogene homolog*) at 6q23.3 is a transcription factor essential for haematopoiesis[1].

The long arm of chromosome 6 (6q) is frequently involved in chromosomal abnormalities in human cancer, including haematological malignancies[1]. Deletions of chromosome 6q are found in acute lymphoblastic leukaemia (ALL), chronic lymphocytic leukaemia (CLL) and high grade nodal and extranodal B-cell lymphoma, but also in breast carcinoma, melanoma, ovarian carcinoma and renal cell carcinoma[2,3].

Additionally, rearrangements involving MYB have been reported in T-ALL, for example the t(6;7)(q23;q34) translocation involving TRB seen in approximately 6% of patients, and focal duplications of the MYB locus, which are present in about 10% of patients[1,4].



REFERENCES

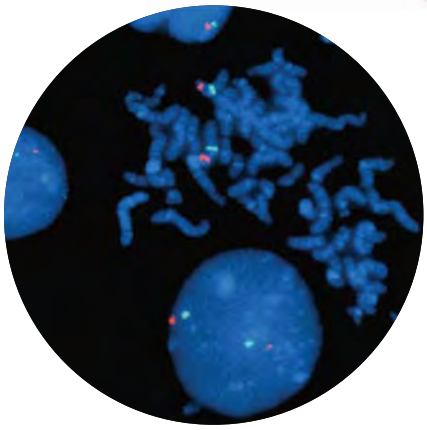
1. Clappier *et al*., Blood 2007;110(4):1251-1261
2. Starostik *et al*., Blood 2000;95(4):1180-1187
3. Stilgenbauer *et al*., Leukemia,1999;13:1331-1334
4. Van Vlierberghe and Ferrando, J of Clin Inv 2012;122(10):3398-3406

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 009-S** (5 tests)
Cat. No. **LPH 009** (10 tests)

P16 (CDKN2A) Deletion*



ALL L **

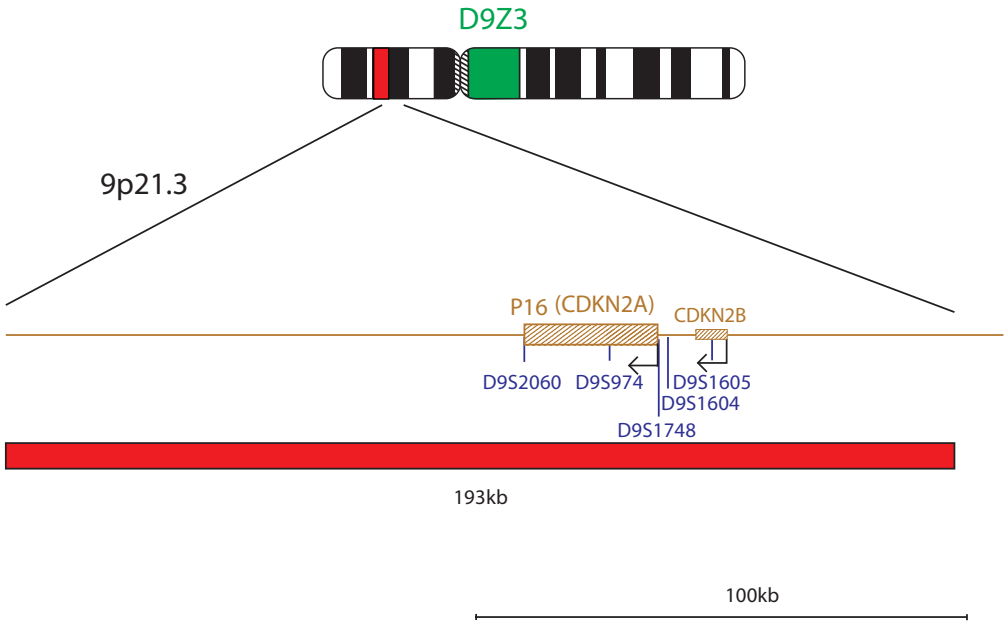
The CDKN2A (*cyclin-dependent kinase inhibitor 2A*) gene at 9p21 is a tumour suppressor gene that has been shown to be deleted in wide range of human malignancies.

Loss of the CDKN2A gene results in cellular proliferation and dysregulation of pro-apoptotic pathways. There are two proteins produced by the CDKN2A gene: $p16^{INK4a}$ and $p14^{ARF}$, these protein products have been linked to two tumour suppressor pathways: the RB pathway and the p53 pathway, respectively[1].

Deletions of 9p that include the CDKN2A gene are frequently reported in patients with acute lymphoblastic leukaemia (ALL): in approximately 30% of adult B-cell ALLs, 30% of childhood ALLs and up to 50% of T-cell ALLs. In adult B-cell ALL, CDKN2A deletions are frequently acquired in disease progression[2,3,4,5].

Deletions including the CDKN2A locus have been reported in up to a third of patients with diffuse large B-cell lymphoma (DLBCL)[6] and, in glioma, CDKN2A loss has been implicated with shorter overall survival in WHO grade I-III astrocytomas[7].

Losses of the CDKN2A region have also been reported in malignant mesothelioma, melanoma, and bladder cancer[8,9,10].



REFERENCES

1. Møller MB, *et al*. Leukemia. 1999 Mar;13(3):453-9
2. Moorman A V, *et al*. Blood. 2007;109(8):3189-97
3. Sulong S, *et al*. Blood. 2014;113(1):100-7
4. Schwab CJ, *et al*. Haematologica .2013 Jul;98(7):1081-8
5. Xu N, *et al*. J Cancer. 2015;6(11):1114-20
6. Jardin F, *et al*., Blood. 2010;116(7):1092-104
7. Reis GF, *et al*. J Neuropathol Exp Neurol. 2015 May;74(5):442-52
8. Conway C, *et al*. Genes Chromosomes Cancer. 2010 May;49(5):425-38
9. Relan V, *et al*. PLoS One. 2013;8(3):e58132
10. Stadler WM, *et al*. Clin Cancer Res. 2001;7(6):1676-82

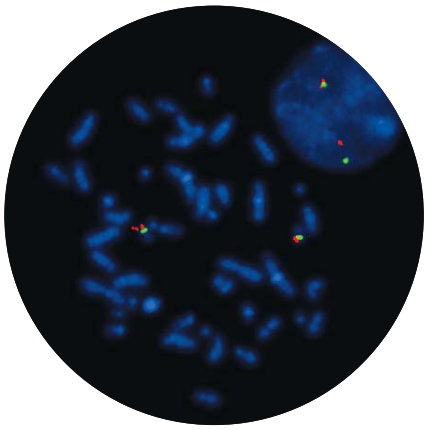
*** A similar product is also available within the Haematopathology range, refer to page 94.**

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 017-S** (5 tests)
Cat. No. **LPH 017** (10 tests)

P53 (TP53) Deletion*



AML CLL L MM ALL **

The TP53 (*tumor protein p53*) gene at 17p13.1 is a tumour-suppressor gene that has been shown to be deleted in a wide range of human malignancies.

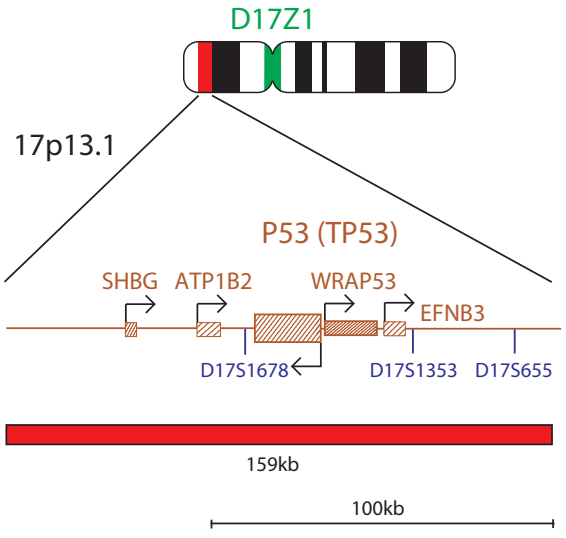
The TP53 gene is one of most important tumour suppressor genes; it acts as a potent transcription factor with fundamental role in the maintenance of genetic stability. Screening for TP53 loss is important as deletions or losses of the short arm of chromosome 17, which includes the TP53 region, are reported in many cancers and are often associated with disease progression, inferior response to treatment and/or a poor prognosis.

In particular, loss of TP53 is reported in 10% of patients with chronic lymphocytic leukaemia (CLL), and is considered to be the poorest prognostic marker in that disease[1,2]. In acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL), TP53 loss is associated with a poor outcome and is often seen as a marker of disease progression or secondary disease[3-5].

TP53 loss in patients with multiple myeloma is a late event, where is seen as a marker of disease progression and is associated with a very poor prognosis[6,7].

In non-Hodgkin lymphoma, TP53 losses are reported in diffuse large B-cell lymphoma (DLBCL) often as part of 'dual-hit' lymphoma or plasmablastic phenotypes[8]. In mantle cell lymphoma (MCL), TP53 losses are associated with a poor outcome, and with a dismal outcome when seen with concurrent CDKN2A deletions[9].

TP53 loss has been reported in a wide range of solid tumour types including gastric cancer[9], breast cancer[10], and non-small cell lung cancer[11].



REFERENCES

1. Rossi D, et al. Blood. 2013 Feb 21;121(8):1403-12
2. Baliakas P, et al. Leukemia. 2014;(April):1-8
3. Grimwade D, et al. Br J Haematol. 2010; (3):17
4. Seifert H, et al. Leukemia. 2009;23(4):656-63
5. Stengel A, et al. Blood. 2014;124(2):251-8
6. Palumbo A, et al. J Clin Oncol. 2015 Sep 10;33(26):2863-9
7. Fonseca R, et al. Leukemia. 2009 Dec;23(12):2210-21
8. Simonitsch-Klupp I, et al. Leukemia. 2004 Jan;18(1):146-55
9. Khayat AS, et al. BMC Gastroenterol. 2009;9:55
10. Liu JC, et al. EMBO Mol Med. 2014 Dec;6(12):1542-60
11. Mogi A, Kuwano H. J. Biomed Biotechnol. 2011;2011:583929

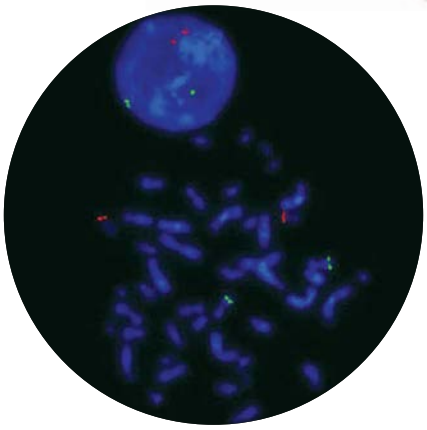
*** A similar product is also available within the Haematopathology range, refer to page 95.**

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 052-S** (5 tests)
Cat. No. **LPH 052** (10 tests)

P53 (TP53)/ATM Probe Combination



CLL **

The tumour suppressor TP53 (*tumor protein p53*) gene at 17p13.1 and the protein kinase ATM (*ataxia-telangiectasia mutated*) gene at 11q22.3, are frequently deleted in cases of chronic lymphocytic leukaemia (CLL).

CLL is the most common leukaemia in adults; its course can vary from very indolent to rapidly progressive. Due to the low mitotic activity of the leukaemic cells *in vitro*, clonal chromosomal abnormalities are detected in 40-50%[2] of cases by conventional cytogenetics using B-cell mitogens, whereas FISH analysis identifies chromosomal aberrations in approximately 80% of CLLs[2]. Screening for deletions of ATM and/or TP53 is vital to allow informed therapy choices for CLL patients, as deletions of TP53 and ATM confer poorer prognosis in this disease[1,2,3].

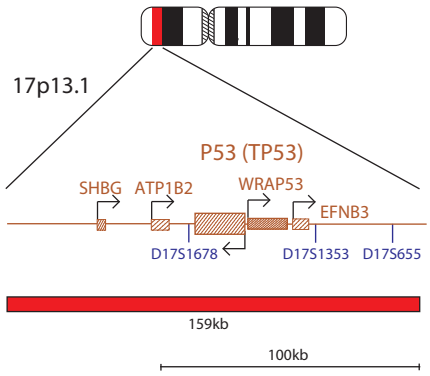
The TP53 gene is one of most important tumour suppressor genes; it acts as a potent transcription factor with fundamental role in the maintenance of genetic stability. Loss of TP53 is reported in 10% of patients with CLL, and is considered to be the poorest prognostic marker in that disease[1,4].

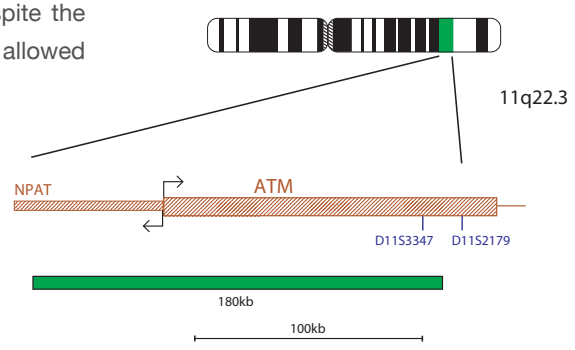
ATM is an important checkpoint gene involved in the management of cell damage and its function is to assess the level of DNA damage in the cell and attempt repair by phosphorylating key substrates involved in the DNA damage response pathway[5]. Loss of ATM is reported in 18% of patients with CLL, and is considered a poor prognostic marker in that disease[2].

Analysis of the ATM/TP53 interaction in CLL has shown that TP53 and ATM play an important role in the proliferation of lymphoid cancer[5], It has been shown that ATM enhances the phosphorylation of TP53, should the damage be so great that the cell requires destruction by apoptosis (which is mediated by TP53). Deletion of ATM removes this checkpoint activity and hence activation of TP53. Thus, there is no attempt made to repair, or apoptosis of, damaged cells, despite the presence of TP53. In the absence of ATM, damaged cells are allowed to continue to proliferate[6].

REFERENCES

1. Rossi D, *et al*. Blood. 2013 Feb 21;121(8):1403-12
2. Dohner *et al*., N Eng J Med 2000;343:1910-1916
3. Zent *et al*., Blood 2010;115(21):4154-4155
4. Baliakas P, *et al*. Leukemia. 2014;(April):1-8
5. Stankovic *et al*., Blood 2004;103(1):291-300
6. Khanna *et al*., Nature Genetics 1998;20(4):398-400



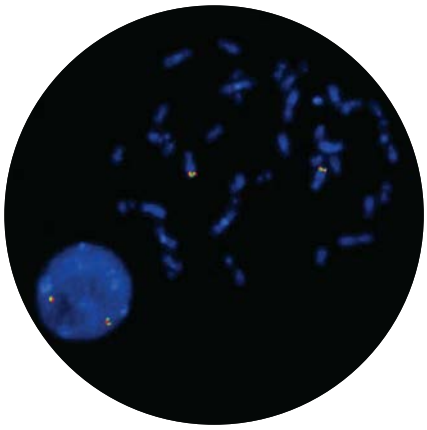


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 031-S** (5 tests)
Cat. No. **LPH 031** (10 tests)

PDGFRB Breakapart



ALL MPN **

Rearrangements involving the PDGFRB (*platelet derived growth factor receptor beta*) gene at 5q32 are reported in both myeloid and lymphoid neoplasms.

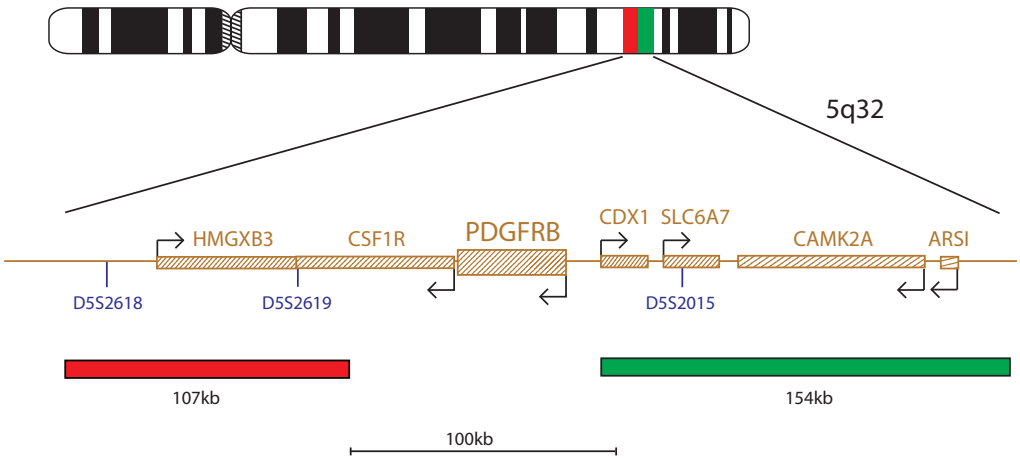
In the 2008 World Health Organization (WHO) classification of myeloid neoplasms and acute leukaemia, a new subgroup of myeloid neoplasms was introduced: *Myeloid and Lymphoid Neoplasms with Eosinophilia and Abnormalities of PDGFRA, PDGFRB or FGFR1*. These neoplasms constitute three specific disease groups, with some shared features[1].

The myeloid neoplasms with PDGFRB rearrangements are characterised by constitutive activation of the PDGFRB gene product[1]. The activation is most commonly caused by a t(5;12)(q31-q33;p13) translocation which results in an ETV6-PDGFRB fusion gene. Patients with this fusion have been shown to be responsive to tyrosine kinase inhibitors (TKIs)[2], which specifically inhibits the kinase activity of PDGFRB.

In B-ALL, gene expression profiling has identified an unusual genetic subgroup, the BCR-ABL1-like or Philadelphia chromosome-like (Ph-like) ALL, which represents about 15% of paediatric ALL cases and has an unfavourable outcome[3,4]. Patients with this expression signature are characterised by genetic alterations, such as rearrangements, mutations and deletions of a range of kinase and cytokine receptors, including PDGFRB rearrangements. Known PDGFRB partners are EBF1 at 5q33, SSBP2 at 5q14, TNIP1 at 5q33 and ZEB2 at 2q22. It is crucial to detect such rearrangements, as patients could benefit from treatment with TKIs[3,4,5].

REFERENCES

1. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France, IARC:2008
2. Apperley JF *et al*., N Engl J Med 2002;347:481
3. Harrison, Hematology Am Soc Hematol Educ Program. 2013;2013:118-125
4. Mullighan, J Clin Invest 2012;122(10):3407-3415
5. Roberts *et al*., N Eng J Med 2014;371(11):1005-1015



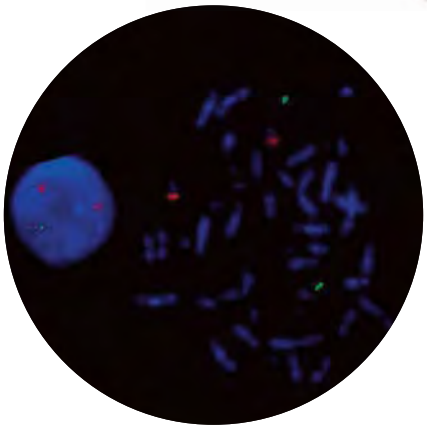
** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 064-S** (5 tests)

Cat. No. **LPH 064** (10 tests)

FAST PML/RARα (RARA) Translocation, Dual Fusion



AML **

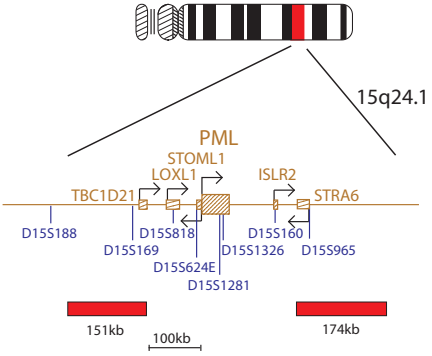
The PML (*promyelocytic leukemia*) gene is located at 15q24.1 and the RARA (*retinoic acid receptor, alpha*) gene is located at 17q21.2. The translocation t(15;17)(q24;q21) gives rise to the PML-RARA fusion gene and is the diagnostic hallmark of acute promyelocytic leukaemia (APL).

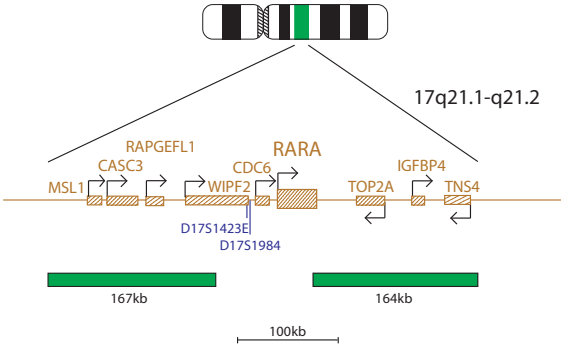
This FAST PML/RARα FISH probe allows rapid detection of the rearrangement, with only one hour of hybridisation required.

The PML-RARA fusion gene is created by the t(15;17)(q24;q21) translocation, found in more than 90% of cases of APL, a leukaemia that comprises 5-8% of cases of acute myeloid leukaemia (AML)[1,2]. In a subset of cases, variant RARA translocations can be observed. Known fusion partners include NPM1 at 5q35, NUMA1 at 11q13, ZBTB16 (PLZF) at 11q23, STAT5B at 17q21, PRKARIA at 17q24, FIP1L1 at 4q12 and BCOR at Xp11[3,4,5].

PML and RARA have both been implicated in normal haematopoiesis. PML possesses growth suppressor and proapoptotic activity whereas RARA is a transcription factor that mediates the effect of retinoic acid at specific response elements[6]. PML-RARA fusion protein behaves as an altered retinoic acid receptor with an ability of transmitting oncogenic signaling[7].

Immediate treatment of APL patients is critical, due to fatal coagulation disorders and life-threatening haemorrhage in diagnosis. Prior to the introduction of all-trans-retinoic-acid (ATRA) and arsenic trioxide (ATO) in APL treatment protocols, the disease had a poor prognosis; however, since the introduction of these therapies, the overall survival rate has improved dramatically, with nearly 90%[5] of patients cured. Patients with variant RARA translocations show variable sensitivity to treatment, with some patients showing resistance to treatment protocols[3,5]. It is therefore important to differentiate between APL patients with PML-RARA fusion and those patients with variant RARA translocations.





** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

REFERENCES

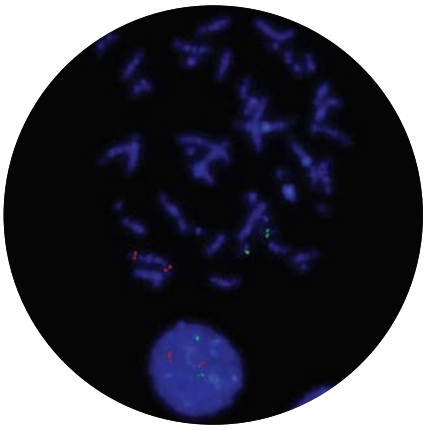
1. Swerdlow *et al.*,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France, IARC:2008
2. Campbell *et al.*, Biomed Research International 2013;2013:1-5
3. Creutzig *et al.*, Blood 2012;120(16):3187-3205
4. Zhang *et al.*, Blood Reviews 2015;29(2):101-125
5. Tomita *et al.*, International Journal of Haematology 2013;97(6):717-725
6. Grimwade *et al.*, Blood 2000;96(4):1297-1308
7. Lo-Coco, Hasa,, Best practice & research. Clinical haematology 2014;27(1):3-9

Cytocell an OGT company aquarius

Cat. No. **LPH 023-S** (5 tests)

Cat. No. **LPH 023** (10 tests)

PML/RARα (RARA) Translocation, Dual Fusion



AML **

The PML (*promyelocytic leukemia*) gene is located at 15q24.1 and the RARA (*retinoic acid receptor, alpha*) gene is located at 17q21.2. The translocation t(15;17)(q24;q21) gives rise to the PML-RARA fusion gene and is the diagnostic hallmark of acute promyelocytic leukaemia (APL).

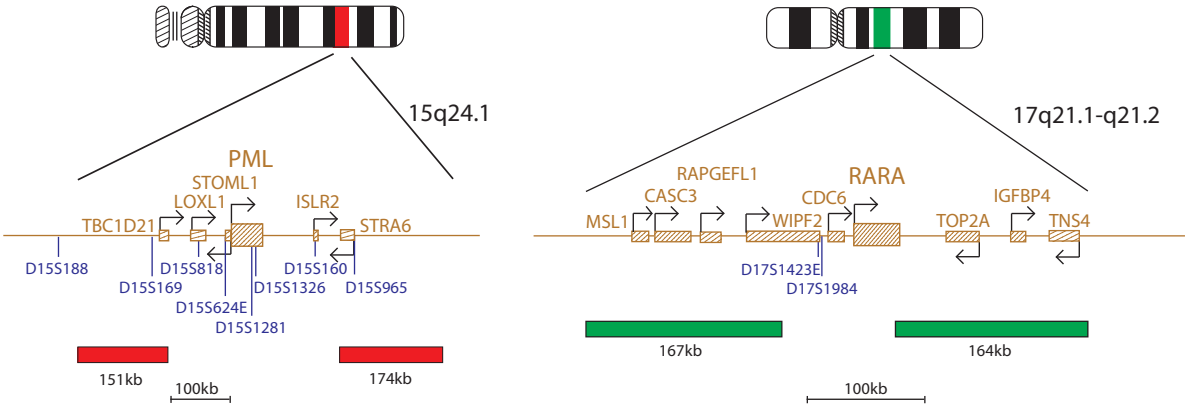
The PML-RARA fusion gene is created by the t(15;17)(q24;q21) translocation, found in more than 90% of cases of APL, a leukaemia that comprises 5-8% of cases of acute myeloid leukaemia (AML)[1,2]. In a subset of cases, variant RARA translocations can be observed. Known fusion partners include NPM1 at 5q35, NUMA1 at 11q13, ZBTB16 (PLZF) at 11q23, STAT5B at 17q21, PRKARIA at 17q24, FIP1L1 at 4q12 and BCOR at Xp11[3,4,5].

PML and RARA have both been implicated in normal haematopoiesis. PML possesses growth suppressor and proapoptotic activity whereas RARA is a transcription factor that mediates the effect of retinoic acid at specific response elements[6]. PML-RARA fusion protein behaves as an altered retinoic acid receptor with an ability of transmitting oncogenic signaling[7].

Immediate treatment of APL patients is critical, due to fatal coagulation disorders and life-threatening haemorrhage in diagnosis. Prior to the introduction of all-trans-retinoic-acid (ATRA) and arsenic trioxide (ATO) in APL treatment protocols, the disease had a poor prognosis; however, since the introduction of these therapies, the overall survival rate has improved dramatically, with nearly 90%[5] of patients cured. Patients with variant RARA translocations show variable sensitivity to treatment, with some patients showing resistance to treatment protocols[3,5]. It is therefore important to differentiate between APL patients with PML-RARA fusion and those patients with variant RARA translocations.

REFERENCES

1. Swerdlow *et al.*,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France, IARC:2008
2. Campbell *et al.*, Biomed Research International 2013;2013:1-5
3. Creutzig *et al.*, Blood 2012;120(16):3187-3205
4. Zhang *et al.*, Blood Reviews 2015;29(2):101-125
5. Tomita *et al.*, International Journal of Haematology 2013;97(6):717-725
6. Grimwade *et al.*, Blood 2000;96(4):1297-1308
7. Lo-Coco, Hasa,, Best practice & research. Clinical haematology 2014;27(1):3-9

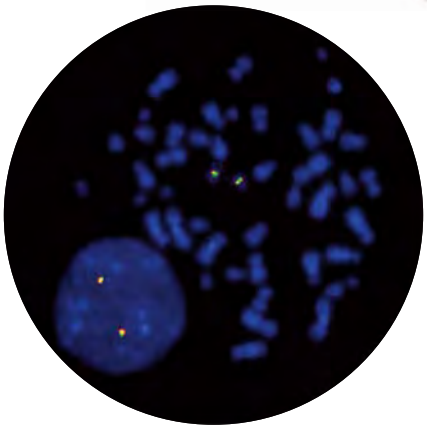


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 065-S** (5 tests)
Cat. No. **LPH 065** (10 tests)

RARα (RARA) Breakapart



The PML (*promyelocytic leukemia*) gene is located at 15q24.1 and the RARA (*retinoic acid receptor, alpha*) gene is located at 17q21.2. In the vast majority of acute promyelocytic leukaemia (APL) cases, the RARA gene at 17q21.2 fuses with PML gene at 15q24.1; however, in <5% of cases of APL, RARA is fused to alternative partner[1].

Known variant fusion partners include NPM1 at 5q35, NUMA1 at 11q13, ZBTB16 (PLZF) at 11q23, STAT5B at 17q21, PRKARIA at 17q24, FIP1L1 at 4q12 and BCOR at Xp11[1,2,3].

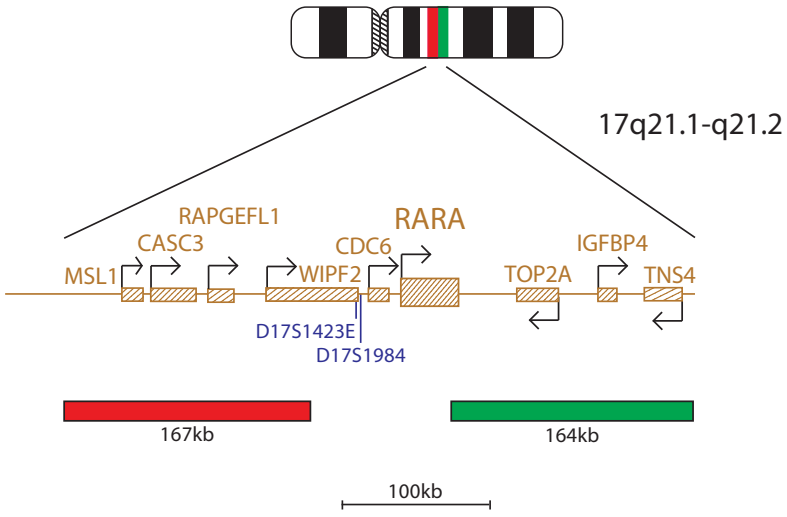
Patients with variant RARA translocations may show variable sensitivity to treatment with some patients showing resistance to treatment protocols[1,3]. It is therefore important to differentiate between APL patients with PML-RARA fusion and those patients with variant RARA translocations.

This breakapart probe will detect rearrangements of the RARA gene, irrespective of partner genes or chromosomes involved.

AML **

REFERENCES

1. Creutzig *et al*., Blood 2012;120(16):3187-3205
2. Zhang *et al*., Blood Reviews 2015;29(2):101-125
3. Tomita *et al*., International Journal of Haematology 2013;97(6):717-725

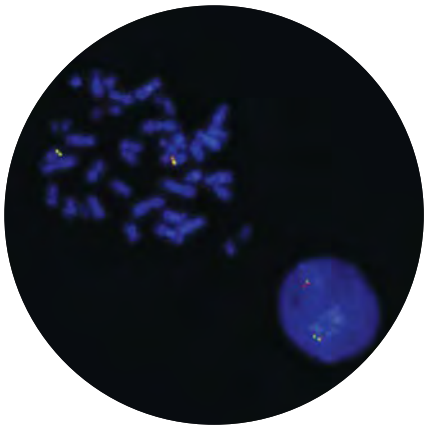


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 046-S** (5 tests)
Cat. No. **LPH 046** (10 tests)

TCL1 Breakapart

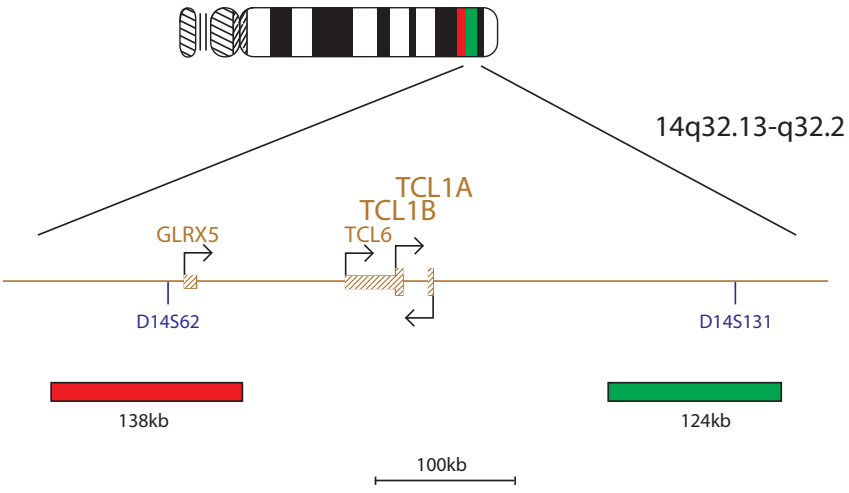


ALL **

The TCL1A (*T-cell leukemia/lymphoma 1A*) and TCL1B (*T-cell leukemia/lymphoma 1B*) genes at 14q32 have been shown to be dysregulated through close juxtaposition of enhancer elements of the T-cell receptor (TCR) genes[1].

Dysregulation of gene transcription is a feature of all acute leukaemias. In T-cell neoplasms, this is brought about by altered expression of normal transcription factor proteins, often as a consequence of chromosomal rearrangements placing these genes into close proximity of the promoter and enhancer elements of the TCR genes: TRA and TRD at 14q11.2, TRB at 7q34 and TRG at 7p14[2,3].

In T-cell prolymphocytic leukaemia (T-PLL) the T-cell Leukaemia 1A/1B gene cluster on chromosome 14q32 has been shown to be involved in a number of different chromosomal rearrangements, including the t(14;14)(q11;q32) and inv(14)(q11;q32), which bring elements of the cluster into close juxtaposition to, and under the control of, the TCR gene promoters and enhancers. There are two breakpoint regions in the gene cluster, each of which are observed in different neoplasms, though both are involved in either the inv(14) or t(14;14). Breakpoints are concentrated in regions centromeric and telomeric to the TCL1A, TCL6 and TCL1B genes[4].

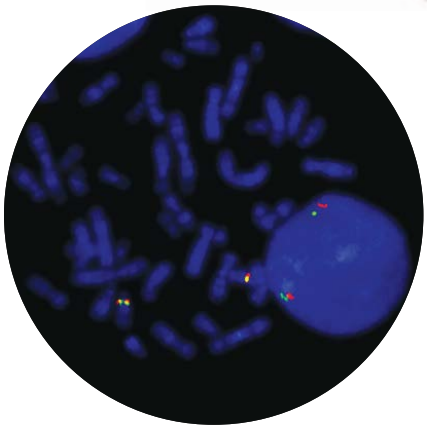


REFERENCES

1. Saitou *et al*., Oncogene 2000;19:2796-2802
2. Korsmeyer SJ, Annual Rev Immunol 1992;10:785-807
3. Gesk *et al*., Leukemia 2003;17:738-745
4. Saitou *et al*., Oncogene 2000;19:2796-802

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

TCRAD Breakapart



ALL **

Chromosomal translocations with breakpoints in alpha and delta T-cell receptor (TCR) gene loci at 14q11.2 are recurrent in several T-cell malignancies including T-cell acute lymphoblastic leukaemia (T-ALL)[1].

T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive malignancy of the lymphoblasts committed to the T-cell lineage and represents 15% of childhood and 25% of adult ALL[2,3]. Karyotyping reveals recurrent translocations that activate a small number of oncogenes in 25-50% of T-ALLs but, with FISH, further cryptic abnormalities can be revealed[2].

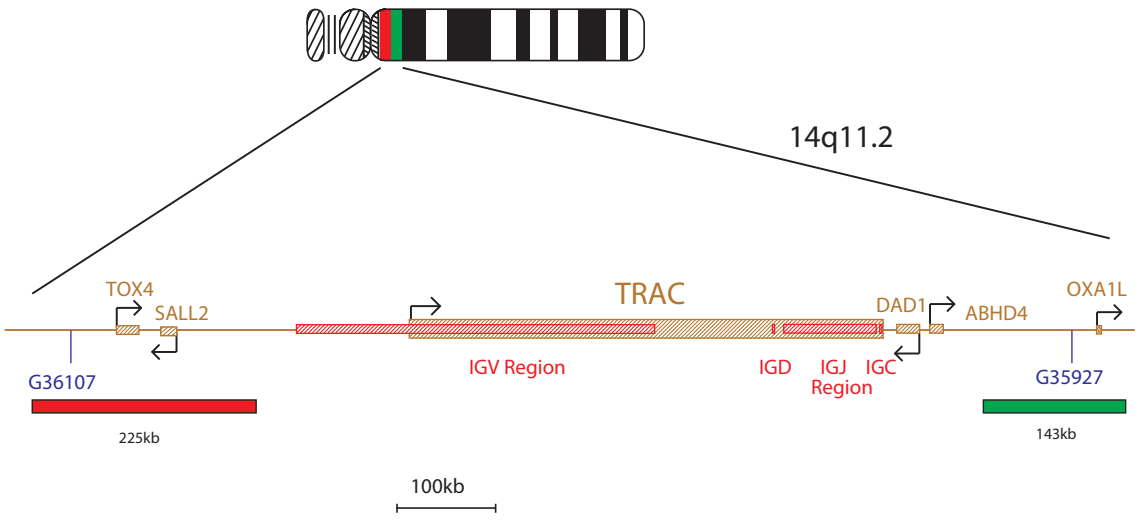
The most common chromosomal rearrangements, found in approximately 35%[2] of T-ALLs, involve the alpha and delta T-cell receptor loci (TRA and TRD) at 14q11.2, the beta TCR locus (TRB) at 7q34 and the gamma TCR (TRG) at 7p14. In most cases the juxtaposition of oncogenes next to the TCR regulatory sequences leads to the deregulated expression of these genes[2,4,5].

The TRA/D complex at 14q11.2 has been shown to be involved in a number of different translocations in T-ALL. These include the t(10;14)(q24;q11) involving TLX1; the t(1;14)(p32;q11) involving TAL1; the t(14;21)(q11;q22) involving the OLIG2; the t(11;14)(p15;q11) involving LMO1 and the t(11;14)(p13;q11) involving LMO2[2].

In addition to T-ALL, TRA/D translocations are recurrent in T-non-Hodgkin's lymphoma and T-prolymphocytic leukaemia. They have also been reported in cases of ataxia telangiectasia (AT)[1].

REFERENCES

1. Rack *et al*., Blood 1997;90(3):1233-1240
2. Graux *et al*., Leukemia 2006;20:1496-1510
3. Cauwelier *et al*., Leukemia 2007;21:121-128
4. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon, France, IARC:2008
5. Gesk *et al*., Leukemia 2003;17:738-745

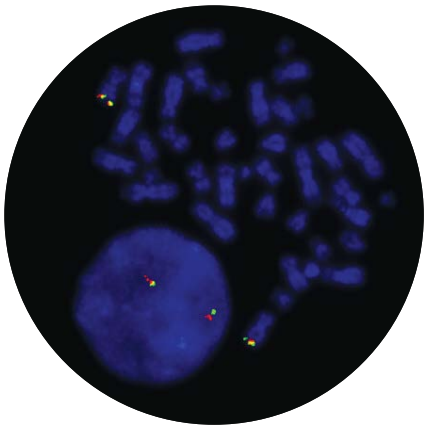


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 048-S** (5 tests)
Cat. No. **LPH 048** (10 tests)

TCRB (TRB) Breakapart



ALL **

Chromosomal translocations with breakpoints in beta T-cell receptor (TCR) gene loci at 7q34 are recurrent in several T-cell malignancies including T-cell acute lymphoblastic leukaemia (T-ALL)[1].

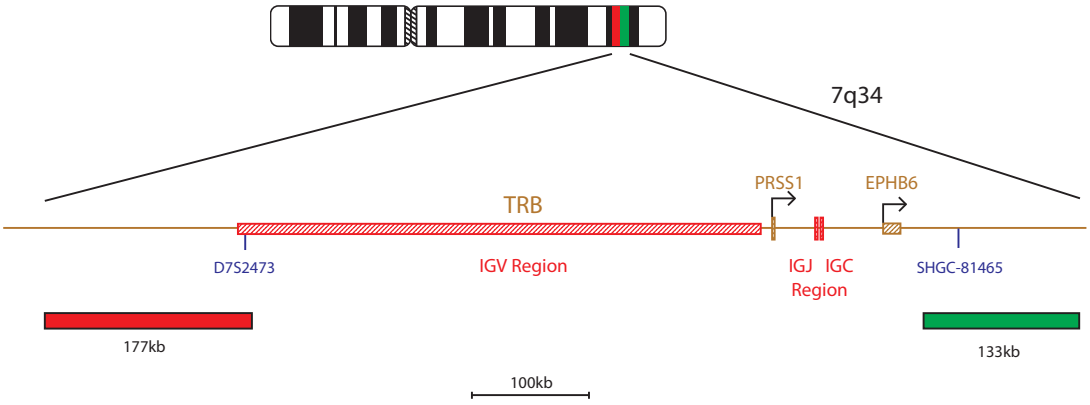
T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive malignancy of the lymphoblasts committed to the T-cell lineage and represents 15% of childhood and 25% of adult ALL[2,3]. Karyotyping reveals recurrent translocations that activate a small number of oncogenes in 25-50% of T-ALLs but with FISH further cryptic abnormalities can be revealed[2].

The most common chromosomal rearrangements, found in approximately 35%[2] of T-ALLs, involve the alpha and delta T-cell receptor loci (TRA and TRD) at 14q11.2, the beta TCR locus (TRB) at 7q34 and the gamma TCR (TRG) at 7p14. In most cases the juxtaposition of oncogenes next to the TCR regulatory sequences leads to the deregulated expression of these genes[2,4,5].

TRB at 7q34 is rearranged with the genes TLX1 at 10q24, HOX cluster at 7p15, LYL1 at 19p13, TAL2 at 9q32, LCK at 1p34 and NOTCH1 at 9q34 via the t(7;10)(q34;q24); t(7;7)(p15;q34); t(7;19)(q34;p13); t(7;9)(q34;q32); t(1;7)(p34;q34) and t(7;9)(q34;q34) translocations respectively[2].

REFERENCES

1. Rack *et al*., Blood 1997;90(3):1233-1240
2. Graux *et al*., Leukemia 2006;20:1496-1510
3. Cauwelier *et al*., Leukemia 2007;21:121-128
4. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon, France, IARC:2008
5. Gesk *et al*., Leukemia 2003;17:738-745

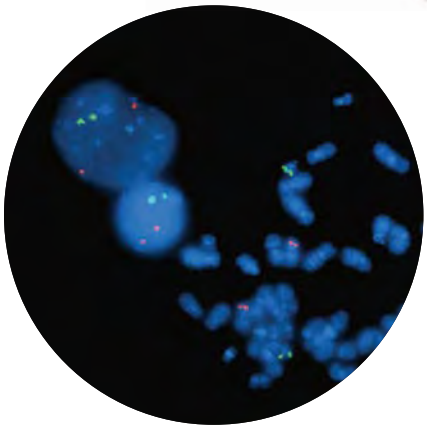


** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 012-S** (5 tests)
Cat. No. **LPH 012** (10 tests)

TEL/AML1 (ETV6/RUNX1) Translocation, Dual Fusion



ALL **

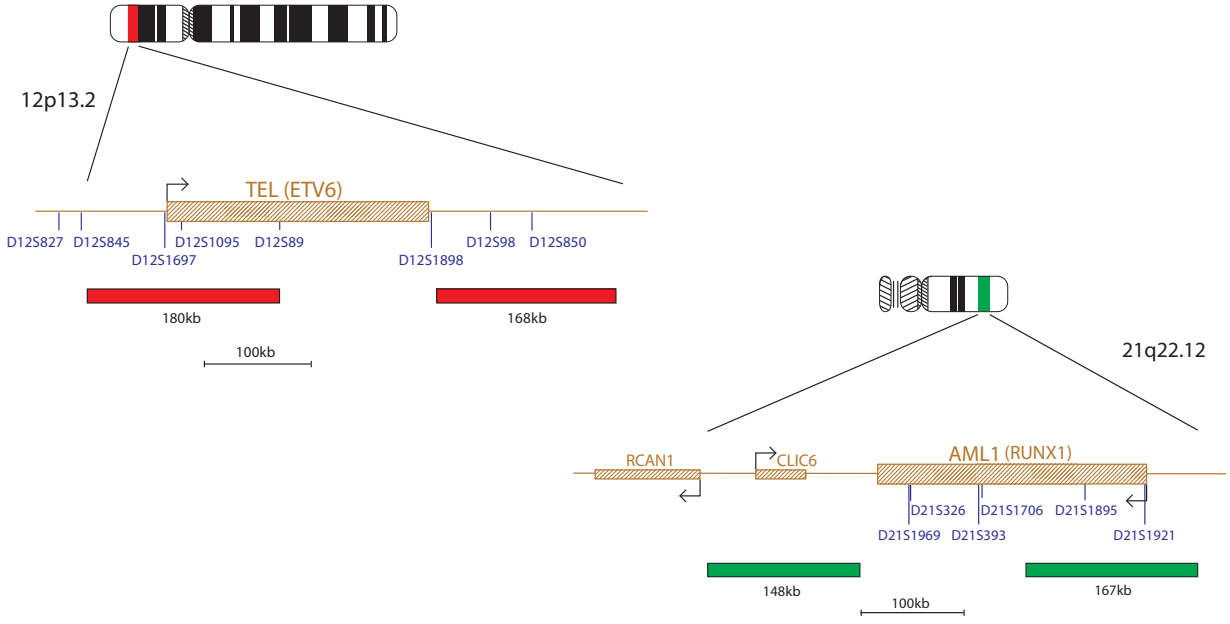
The cytogenetically-cryptic t(12;21)(p13;q22) translocation between ETV6 (*ets variant 6*) at 12p13 and RUNX1, (*runt related transcription factor 1*) at 21q22, results in the ETV6-RUNX1 chimeric fusion gene[1].

The ETV6 and RUNX1 genes both encode transcription factors; ETV6 has been shown to be required for proper transcription during haematopoiesis within the bone marrow [1,2]. The ETV6-RUNX1 protein converts RUNX1 to a transcriptional repressor and causes overexpression of the erythropoietin receptor (EPOR) and activation of downstream JAK-STAT signaling[1].

B-lymphoblastic leukaemia/lymphomas with t(12;21)(p13;q22) translocations form a recognised disease entity according to the World Health Organization (WHO) classification of myeloid neoplasms and acute leukaemia. This is the most common sub-group of childhood B-ALL accounting for about 25% of cases[3]. As the t(12;21)(p13;q22) translocation is cytogenetically-cryptic, FISH is an important diagnostic tool for this leukaemia[4].

B-ALL with ETV6-RUNX1 is considered to have a favourable outcome with cure rates more than 90%[3]. Late relapses have been reported; these have been attributed to the presence of persistent preleukaemic clones that survived chemotherapy[3,5].

ETV6 has also been shown to be deleted in some children with ALL, with loss of heterozygosity (LOH) of chromosome 12p12-13; these deletions often seen in the presence of ETV6-RUNX1 translocations[6].



REFERENCES

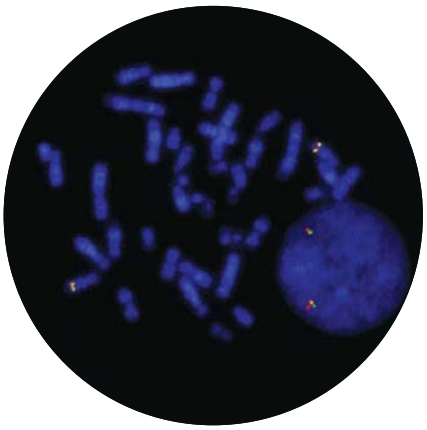
1. Mullighan, The Journal of Clinical Investigation 2012;122(12):3407-3415
2. Wang *et al*., Genes Dev 1998;12(15):2392-2402
3. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France, IARC:2008
4. Borkhardt *et al*., Blood. 1997;90(2):571-577
5. Mosad *et al*., Journal of Haematology & Oncology 2008;1:17
6. Raynaud *et al*., Blood 1996;87(7):2891-2899

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 049-S** (5 tests)
Cat. No. **LPH 049** (10 tests)

TLX1 Breakapart

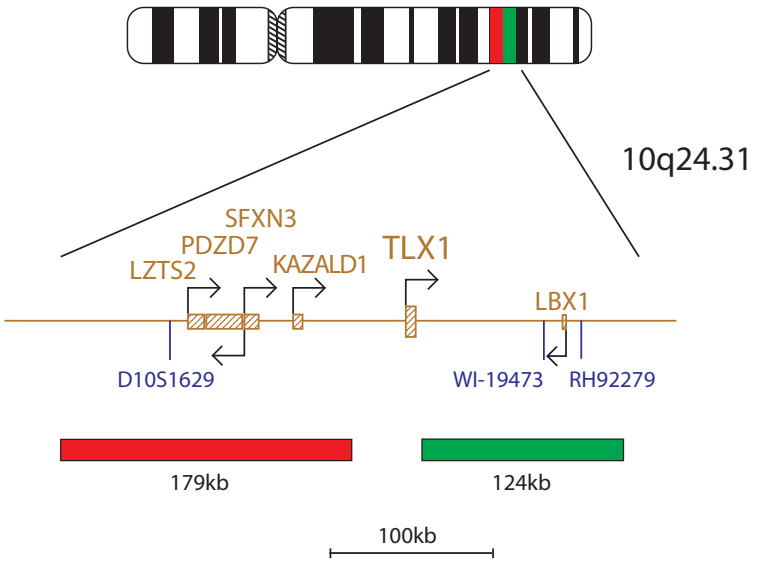


ALL **

The TLX1 (*T-cell leukemia homeobox 1*) gene at 10q24 is aberrantly expressed in 30% of adult and 5-10% of childhood T-cell acute lymphoblastic leukaemia (T-ALL)[1,2].

Dysregulation of gene transcription is a feature of all acute leukaemias. In T-cell neoplasms, this is brought about by altered expression of normal transcription factor proteins, often as a consequence of chromosomal rearrangements placing these genes into close proximity of the promoter and enhancer elements of the TCR genes: TRA and TRD at 14q11.2, TRB at 7q34 and TRG at 7p14[3,4].

Murine studies show that expression of mouse homologues of TLX1 can immortalise haematopoietic cells *in vitro* as the first of a potential two-hit mechanism leading to full malignancy[2]. This work suggests that TLX1 is an oncogene that can become dysregulated via the translocations t(10;14)(q24;q11) or t(7;10)(q35;q24), placing it into close proximity with TRA/D and TRB elements respectively[5]. Additionally, TLX1 is frequently activated in T-ALL in the absence of an overt genetic rearrangement. T-ALLs with TLX1 expression show a more favourable outcome than other T-ALLs[5].



REFERENCES

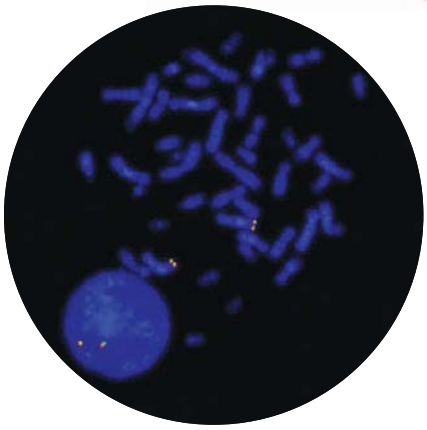
1. Riz *et al*., Oncogene (2005
2. Hawley RG *et al*., Oncogene 1994;9:1-12
3. Korsmeyer SJ, Annual Rev Immunol 1992;10:785-807
4. Gesk *et al*., Leukemia 2003;17:738-745
5. Graux *et al*., Leukemia 2006;20:1496-1510

** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell an OGT company aquarius

Cat. No. **LPH 050-S** (5 tests)
Cat. No. **LPH 050** (10 tests)

TLX3 Breakapart



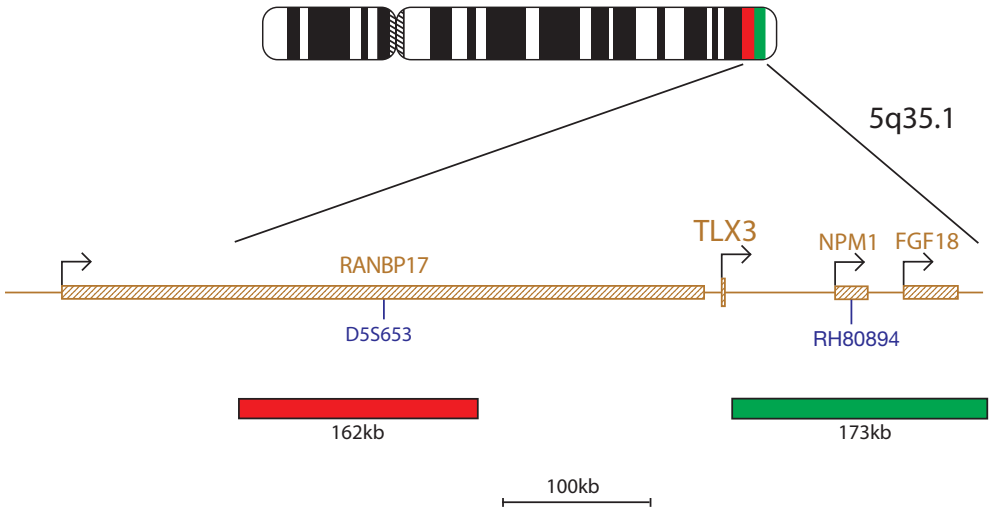
ALL **

The TLX3 (*T-cell leukemia homeobox 3*) gene at 5q35 can be aberrantly expressed in T-cell acute lymphblastic leukaemia (T-ALL) due to a cryptic translocation[1].

Unlike TLX1, the dysregulation of TLX3 is not brought about by close juxtaposition with T-cell receptor genes, instead, it is brought into contact with another gene that is highly expressed in normal T-cell differentiation: BCL11B at 14q32[2]. The t(5;14)(q35;q32) translocation is cryptic and the breakpoint does not actually disrupt TLX3 but, in the majority of cases, occurs within or downstream of the RANBP17 gene[3]. RANBP17 is very close to TLX3 and although its expression is not affected by the translocation, TLX3 expression is affected. The t(5;14)(q35;q32) translocation is found in approximately 20% of childhood T-ALL and 13% of adult cases. Rarer TLX3 rearrangements have also been reported: a t(5;7)(q35;q21) translocation involving CDK6 at 7q21 and a t(5;14)(q35;q11) translocation involving TRA/D at 14q11.2[1].

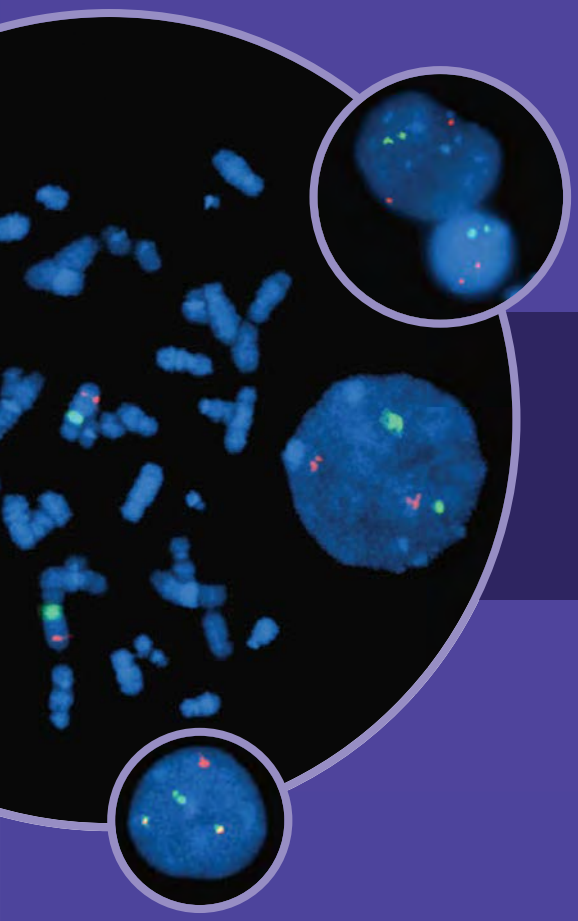
REFERENCES

1. Graux *et al*., Leukemia 2006;20:1496-1510
2. Bernard OA *et al*., Leukaemia 2001;15:1495-504
3. Van Zutven *et al*., Haematologica 2004;89:671-8



** These roundels are only intended to provide information supported by the literature and are not a reflection of the intended purpose of this product.

Cytocell
an OGT company
multiprobe



Multiprobe Haematology

Contents

Multiprobe Haematology

As long ago as the 19th century, nuclear changes were recognised as being significant in cancer biology. Advances in cytogenetics and molecular cytogenetics in the last century showed that although a number of numerical and structural chromosome changes appeared to be random and non-specific, rearrangements involving individual chromosomes were shown to define specific abnormalities in individual tumour types.

Fluorescence *in situ* hybridisation (FISH), using locus-specific probes that are capable of defining these stereotypic structural rearrangements, has now become a routine diagnostic test in the clinical laboratory and the technique has thus been shown to be useful in the management of cancer patients.

The Chromoprobe Multiprobe® haematology devices are designed for use on interphase nuclei and metaphase chromosomes from cultured peripheral blood cells or cultured bone marrow samples.

Multiprobe Overview

The Chromoprobe Multiprobe® System is an extension of Cytocell's proprietary Chromoprobe® technology, whereby DNA FISH probes are reversibly bound to the surface of a glass device. These probes dissolve back into solution once in contact with the supplied hybridisation buffer, whilst denaturation of the probes and target DNA occurs simultaneously under the device once heated. This approach not only simplifies the whole FISH procedure but also renders it safer and quicker to use.

This system allows multiple FISH probes to be hybridised on the same slide in a spatially separated manner allowing rapid screening of a patient sample for a number of different DNA sequences in a single FISH analysis.

The assay is supplied in a kit format of 2, 5 or 10 devices and includes hybridisation solution, DAPI counterstain, template slides, a hybridisation chamber and full instructions for use. The kit even contains a unique liquid crystal display slide surface thermometer for accurate temperature measurement of the denaturation surface.

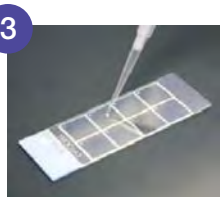
The procedure is simple:

1

Soak the slides in 100% methanol, then polish dry with a lint free cloth.

2

Spot 4µl (or 2µl for a 24 square device) of cell sample onto alternate squares of the supplied slide.

3

Once dry, fill in the remaining squares with the cell sample and check using phase contrast.

4

Place slides in 2xSSC for 2 minutes and then dehydrate through an ethanol series.

5

Spot 2µl (or 1µl for a 24 square device) of supplied hybridisation solution onto each square of the device.

6

Carefully lower spotted slide onto the device.

7

Check the temperature of the hotplate using the slide surface thermometer provided. Denature the slide/device at 75°C for 2 minutes (or 5 minutes for OctoChrome™ device).

8

Place slide/device in hybridisation chamber supplied and float on the surface of a clean 37°C waterbath overnight.

9

Wash in 0.4xSSC at 72°C for 2 minutes, then 2xSSC/0.05% Tween at room temperature for 30 seconds.

10

Apply DAPI counterstain provided and view under a fluorescence microscope.

Chromoprobe Multiprobe® ALL v2

cMYC (MYC) Breakapart

Chromosomal rearrangements involving the MYC (*v-myc avian myelocytomatosis viral oncogene homolog*) gene at 8q24 are recognised recurrent abnormalities commonly seen in patients with B-cell malignancy. MYC rearrangements, activating MYC by translocation with one of the three immunoglobulin loci (IGH, IGL or IGK), are detected in almost all cases of Burkitt lymphoma at diagnosis[1].

TEL/AML1 (ETV6/RUNX1) Translocation, Dual Fusion

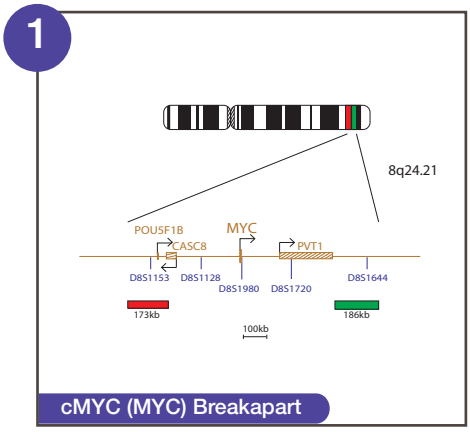
The cytogenetically-cryptic t(12;21)(p13;q22) translocation between ETV6 (*ets variant 6*) at 12p13 and RUNX1, (*runt related transcription factor 1*) at 21q22, results in the ETV6-RUNX1 chimeric fusion gene[2]. This is the most common rearrangement in childhood B-cell acute lymphoblastic leukaemia (B-ALL) accounting for about 25% of cases. B-ALL with ETV6-RUNX1 is considered to have a favourable outcome with cure rates up to 90%. Late relapses have been reported[3].

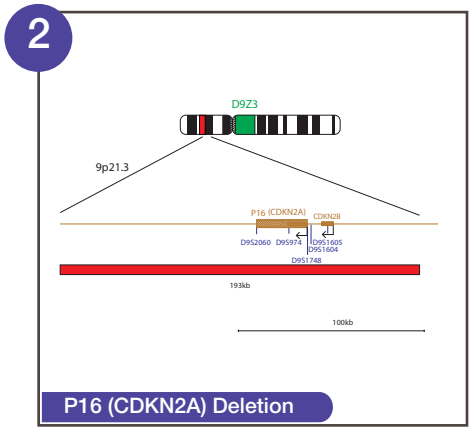
P16 (CDKN2A) Deletion

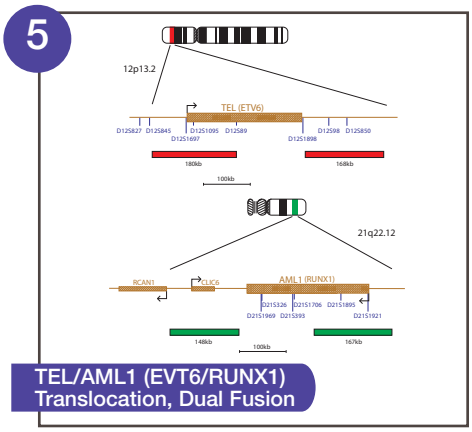
The CDKN2A (*cyclin-dependent kinase inhibitor 2A*) gene at 9p21 is a tumour suppressor gene that has been shown to be deleted in a wide range of human malignancies. Deletions of 9p that include the CDKN2A gene are frequently reported in patients with ALL: in approximately 30% of adult B-cell ALLs, 30% of childhood ALLs and up to 50% of T-cell ALLs. In adult B-ALL, CDKN2A deletions are frequently acquired in disease progression[4,5,6,7].

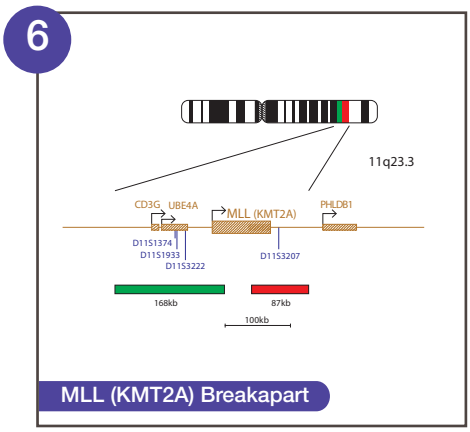
MLL (KMT2A) Breakapart

KMT2A rearrangements can be detected in approximately 80% of infants with acute lymphoblastic leukaemia (ALL) and in 5-10% of paediatric and adult ALLs[8,9]. Historically, KMT2A rearrangements in acute leukaemia were associated with a poorer outcome, but recent studies have shown that the prognosis is highly dependent on the fusion partner and it may differ between children and adults[10].









E2A (TCF3) Breakapart

The TCF3 (*transcription factor 3*) gene is located at 19p13.3. Translocations involving TCF3 are some of the most common rearrangements in childhood B-ALL. The t(1;19)(q23;p13) is the most common TCF3 rearrangement, being present in around 6% of childhood B-ALL[3,8]. The translocation was historically associated with a poor outcome, though modern intensive therapies have overcome this[3,8,11]. The t(17;19)(q22;p13.) is a rare translocation that is present in around 1% of ALL cases[1]. TCF3/HLF positive leukaemia is associated with adverse prognosis[2,11].

BCR/ABL (ABL1) Translocation, Dual Fusion

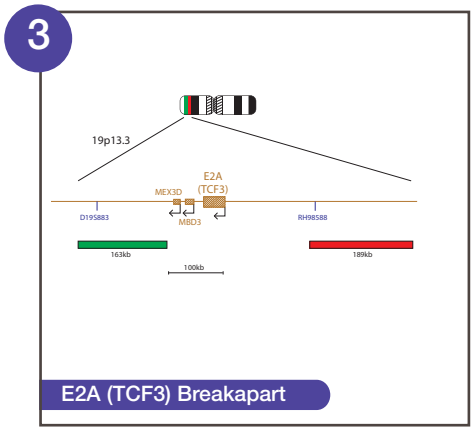
BCR/ABL1 positive ALL has been shown to confer a poor prognosis in both adults and children, thus detection of the abnormality is of high importance for high risk stratification and for treatment and management decisions[12]. In a small number of ALL cases, the translocation does not result in a cytogenetically visible Philadelphia chromosome. In these cases FISH is essential for highlighting the fusion gene[13].

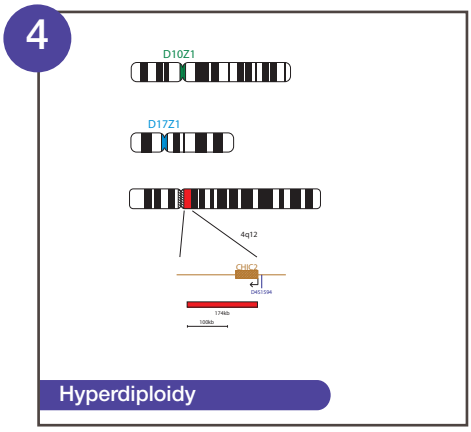
Hyperdiploidy

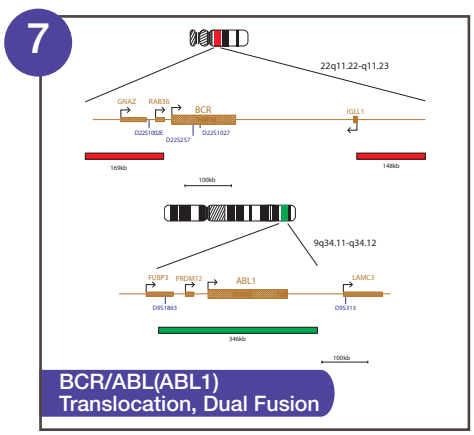
High hyperdiploidy leukaemia (51 – 65 chromosome) is very common in children accounting for about 30% of cases of ALL. It is usually characterised by the gain of specific chromosomes (usually gains of 4,6,10,14, 17,18,21 and X) and is associated with a favourable outcome[3,12,14].

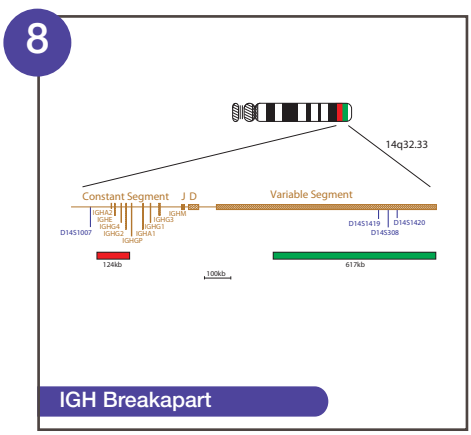
IGH Breakapart

Recurrent rearrangements involving the IGH (*immuno-globulin heavy locus*) gene at 14q32.33 with a wide range of partner genes are seen in haematological malignancies such as ALL[15]. The breakapart design for this probe set allows the detection of rearrangements of the IGH region, regardless of partner gene or chromosome involved.









For a list of references, please see page 80.
For more information please see individual product pages.

Cytocell an OGT company multiprobe

Cat. No. **PMP 018**	(2 devices)	Cat. No. **PMP 016**	(10 devices)
Cat. No. **PMP 017**	(5 devices)	Cat. No. **PMP 020**	(20 devices)

Chromoprobe Multiprobe® CLL

MYB Deletion

The long arm of chromosome 6 (6q) is frequently involved in chromosomal abnormalities in human cancer, including chronic lymphocytic leukaemia (CLL)[1]. The MYB (*v-myb avian myeloblastosis viral oncogene homolog*) is provided as a marker for 6q deletion.

Chromosome 12 Enumeration

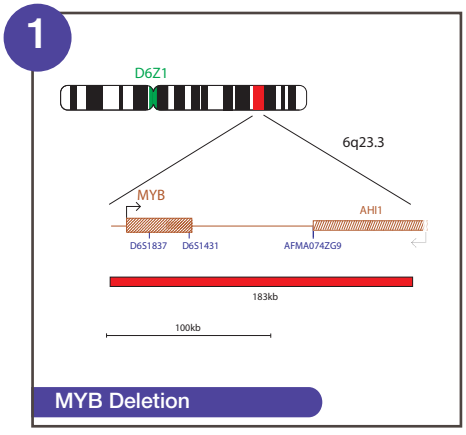
Trisomy 12 is a recurrent abnormality in CLL, seen in 20% of cases[3] that often appears as the unique cytogenetic aberration (40-60% of cases with trisomy 12)[2]. Patients with trisomy 12 are classified as low-risk in the absence of any other genetic lesions[4].

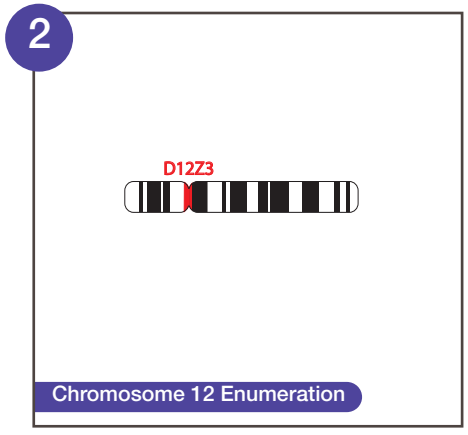
IGH Breakapart

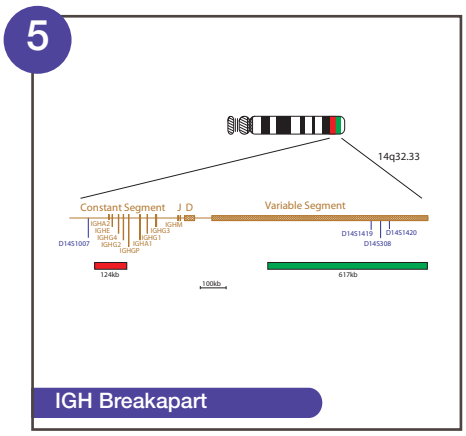
Around 4-9% of CLL patients have a balanced translocation involving IGH. The two most common translocations are IGH/BCL2, caused by the t(14;18) translocation, and IGH/BCL3, a result of the t(14;19) translocation. The prognostic outcome of the translocation is depended on the translocation partner of IGH[2].

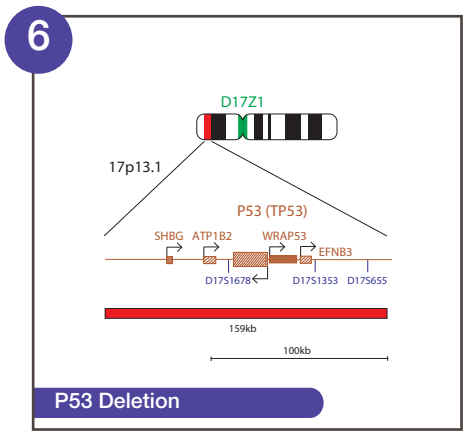
P53 (TP53) Deletion

The TP53 (*tumor protein p53*) gene at 17p13.1 is one of most important tumour suppressor genes; it acts as a potent transcription factor with fundamental role in the maintenance of genetic stability. Loss of TP53 is reported in 10% of patients with CLL, and is considered to be the poorest prognostic marker[4,5].









ATM Deletion

The ATM (*ataxia-telangiectasia mutated*) gene at 11q22.3 is an important checkpoint gene involved in the management of cell damage and its function is to assess the level of DNA damage in the cell and attempt repair by phosphorylating key substrates involved in the DNA damage response pathway[6]. Loss of ATM is reported in 18% of patients with CLL, and is considered a poor prognostic marker in CLL[7].

IGH/CCND1 Translocation, Dual Fusion

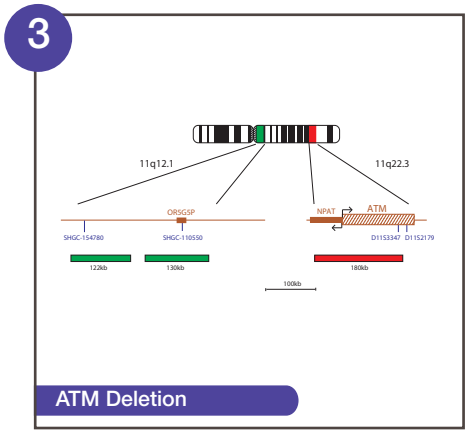
The t(11;14)(q13;q32) rearrangement involving CCND1 and IGH is considered the hallmark of mantle cell lymphoma (MCL)[8], the presence of which can be used to aid in the differential diagnosis of CD5+ B-cell lymphoproliferative disorders[9].

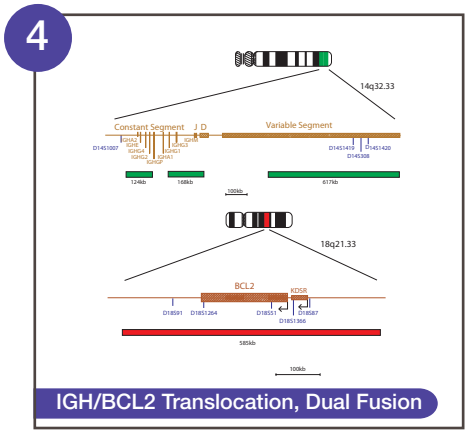
IGH/BCL2 Translocation, Dual Fusion

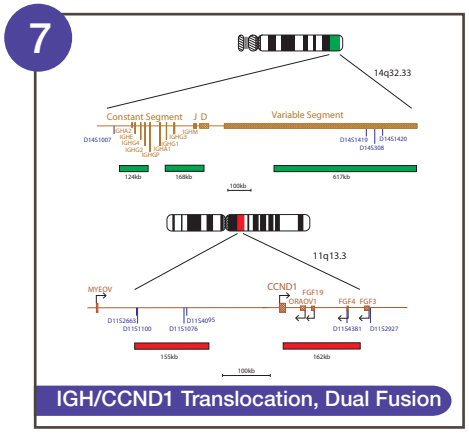
The t(14;18)(q32;q21) translocation involving the IGH (*immunoglobulin heavy locus*) gene at 14q32 and the BCL2 (*B-cell CLL/lymphoma 2*) gene at 18q21.33 is a recognised recurrent abnormality seen in B-cell malignancies, occurring occasionally in CLL[10].

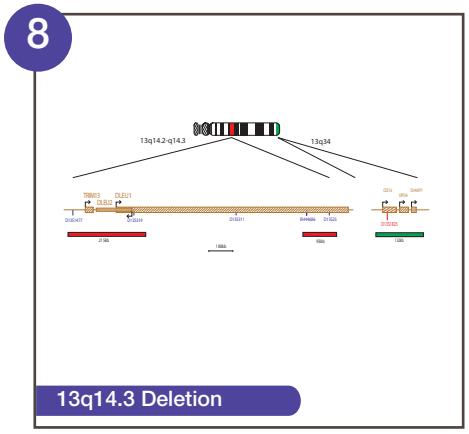
13q14.3 Deletion

Deletions affecting 13q14 are the most frequent structural genetic aberrations in CLL[2,11,12]. This region is found to be heterozygously deleted in 30-60% and homozygously deleted in 10-20% of CLL patients[13]. Patients with 13q14 deletions are classified as very low risk, in the absence of any other genetic lesions[4].









For a list of references, please see page 80.
For more information please see individual product pages.

Cytocell an OGT company multiprobe

Cat. No. **PMP 025**	(2 devices)	Cat. No. **PMP 027**	(10 devices)
Cat. No. **PMP 026**	(5 devices)	Cat. No. **PMP 028**	(20 devices)

Chromoprobe Multiprobe® AML/MDS

Del(5q) Deletion

Deletions of the long arm of chromosome 5 are one of the most common karyotypic abnormalities in myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML) with myelodysplasia related changes[1,2]. This del(5q) probe will detect deletions of EGR1 (*early growth response 1*), a tumor suppressor gene at 5q31. EGR1 has been shown to act through haploinsufficiency to initiate the development of MDS/AML[5].

MLL (KMT2A) Breakapart

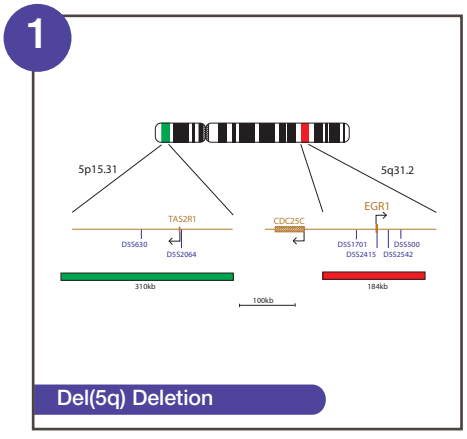
KMT2A rearrangements can be detected in approximately 60% of infant AML and in 3% of de novo and 10% of therapy related adult AML cases[4,5]. Historically, KMT2A rearrangements in acute leukaemia were associated with a poorer outcome, but recent studies have shown that the prognosis is highly dependent on the fusion partner and it may differ between children and adults[6].

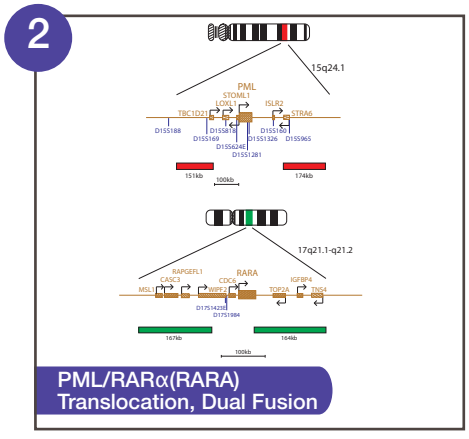
PML/RARα(RARA) Translocation, Dual Fusion

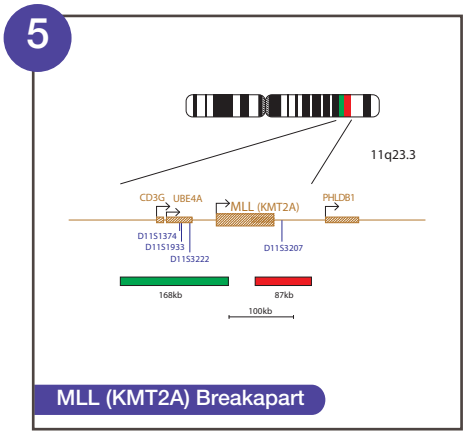
The translocation t(15;17)(q24;q21) gives rise to the PML-RARA fusion gene and is the diagnostic hallmark of acute promyelocytic leukaemia (APL). Immediate treatment of APL patients is critical, due to fatal coagulation disorders and life-threatening haemorrhage in diagnosis. Since the introduction of all-trans-retinoic-acid (ATRA) and arsenic trioxide (ATO) in APL treatment protocols, the overall survival rate has improved dramatically, with nearly 90% of patients cured[7,8].

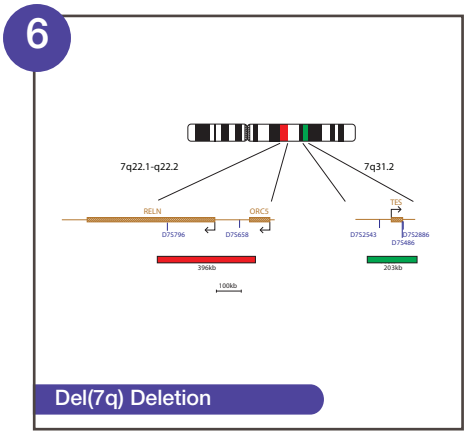
Del(7q) Deletion

Monosomy of chromosome 7 and deletions of the long arm of chromosome 7 are recognised recurrent chromosomal aberrations frequently seen in myeloid malignancies and are associated with poorer outcome[9,10].









P53 (TP53) Deletion

The TP53 (*tumor protein p53*) gene at 17p13.1 is one of most important tumour suppressor genes; it acts as a potent transcription factor with fundamental role in the maintenance of genetic stability. In AML and acute lymphoblastic leukaemia (ALL), TP53 loss is associated with a poor outcome and is often seen as a marker of disease progression or secondary disease[11,12].

AML1/ETO (RUNX1/RUNX1T1) Translocation, Dual Fusion

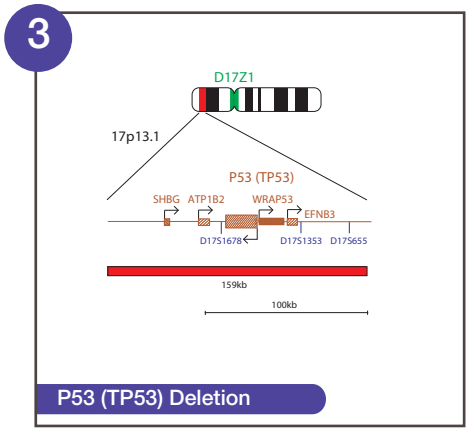
The translocation t(8;21)(q22;q22) gives rise to the RUNX1-RUNX1T1 fusion gene. The translocation is observed in 10-22% of patients with AML FAB type M2 and 5-10% of AML cases overall, most commonly in children and young adults[15] and is a good prognostic indicator[11,16,17].

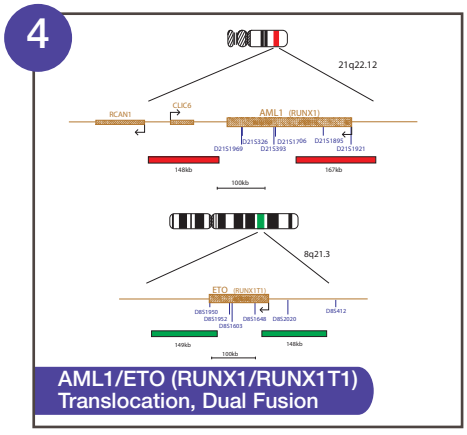
CBFβ/MYH11 Translocation, Dual Fusion

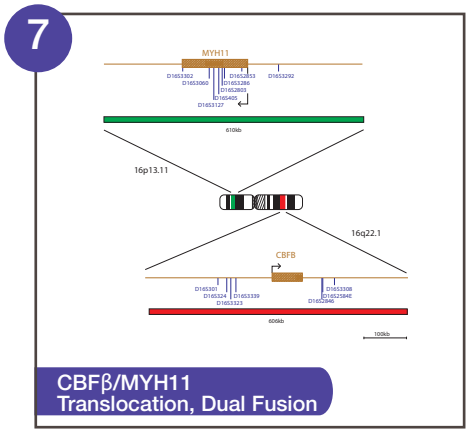
The inversion inv(16)(p13.11;q22.1) and the translocation t(16;16)(p13.11;q22.1) give rise to the CBFB-MYH11 fusion gene. These rearrangements are frequently found in patients with a myelomonocytic subtype with increased bone marrow eosinophils, AML FAB (French-American-British classification) type M4Eo, and are found in 5-8% of all AMLs. Cases of therapy-related AML may also have this rearrangement[2,13]. CBFB-MYH11 rearrangements are classed as a favourable cytogenetic risk group in patients with AML[11,14].

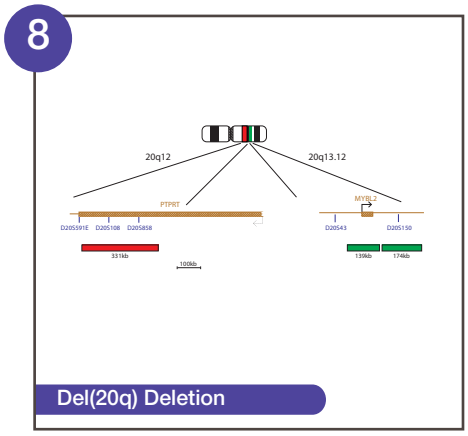
Del(20q) Deletion

Deletions of the long arm of chromosome 20 are a common chromosomal abnormality associated with myeloid malignancies, in particular myelodysplastic syndromes (MDS) and AML[18]. Deletions of 20q can be seen in 4% of MDS cases and in 1-2% of AML cases[19]. The prognosis for MDS where del(20q) is the sole abnormality is good; however, the presence of secondary abnormalities may be indicative of disease progression[20].









For a list of references, please see page 80.
For more information please see individual product pages.

CHROMOPROBE MULTIPROBE® ALL: REFERENCES PAGES 74-75

1. Perkins AS, Friedberg JW. Hematology Am Soc Hematol Educ Program. 2008;341–8.
2. Mullighan, The Journal of Clinical Investigation 2012;122(12):3407-3415
3. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France,IARC:2008
4. Moorman A V, *et al*. Blood. 2007;109(8):3189–97
5. Sulong S, *et al*. Blood. 2014;113(1):100–7
6. Schwab CJ, *et al*. Haematologica .2013 Jul;98(7):1081–8
7. Xu N, *et al*. J Cancer [Internet]. 2015;6(11):1114–20
8. Van der Burg *et al*., Leukemia 2004;18(5):895-908
9. Tomizawa, Pediatr Int 2015;57(8):811-819
10. Tamai, Inokuchi, J Clin Exp Hematopathol 2010;50(2):91-98
11. Moorman *et al*., Lancet Oncol
12. Harrison *et al*., BJH 2010;151:132-142
13. Van Rhee *et al*., Br j Haematol 1995;90:225-8
14. Professional Guidelines for Clinical Cytogenetics: ACUTE LYMPHOBLASTIC LEUKAEMIA BEST PRACTICE GUIDELINES (2011) V1.00. www.cytogenetics.org.uk
15. Gozzetti A, *et al*. Cancer Res.2002 Oct 1;62(19):5523–7

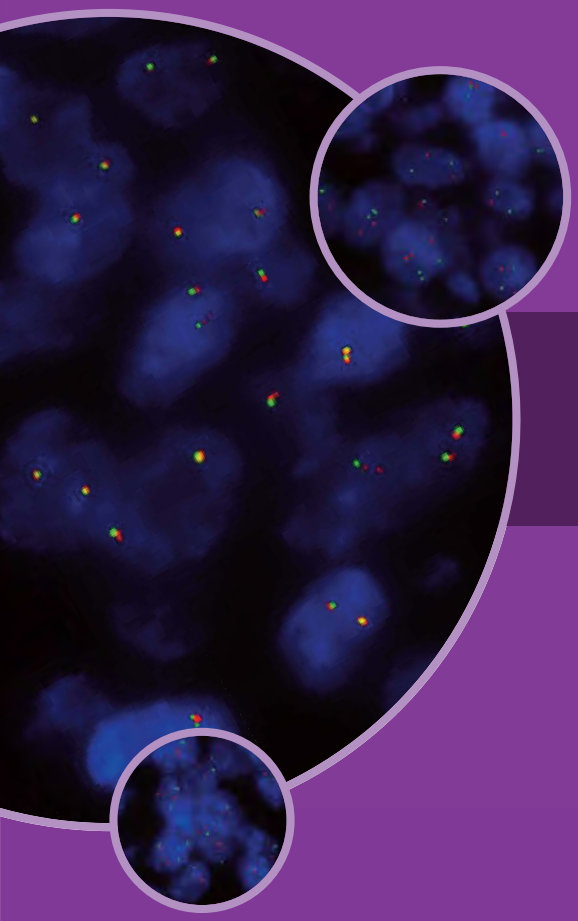
CHROMOPROBE MULTIPROBE® CLL: REFERENCES PAGES 76-77

1. Stilgenbauer *et al*., Leukemia,1999;13:1331-133
2. Puiggros *et al*., Biomed Res Int 2014;1-13
3. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France,IARC:2008
4. Rossi *et al*., Blood 2013;121(8):1403-1412
5. Baliakas P, *et al*. Leukemia. 2014;(April):1–8
6. Stankovic *et al*., Blood 2004;103(1):291-300
7. Dohner *et al*., N Eng J Med 2000;343:1910-1916
8. Vose JM. Am J Hematol. 2013;88(12):1082–8.
9. Ho AK, *et al*.. Am J Clin Pathol 2009;131:27–32.
10. Bassegio L *et al*., Br J Haematol 2012;158(4):489-98
11. Juliusson G *et al*., N Eng J Med 1990;323:720-4
12. Kasar *et al*., Nature Communications 2015;6:1-12
13. Hammarsund M *et al*., FEBS Letters 2004;556:75-80

CHROMOPROBE MULTIPROBE® AML/MDS: REFERENCES PAGES 78-79

1. Ebert, Best Pract Res Clin Haematol 2010;23(4):457-461
2. Swerdlow *et al*.,editors, WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Lyon,France,IARC:2008
3. Joslin *et al*., Blood;110(2):719-726
4. Van der Burg *et al*., Leukemia 2004;18(5):895-908
5. Grossman *et al*., Leukemia 28 March 2013; doi10.1038/leu.2013.90
6. Tamai, Inokuchi, J Clin Exp Hematopathol 2010;50(2):91-98
7. Creutzig *et al*., Blood 2012;120(16):3187-3205
8. Tomita *et al*., International Journal of Haematology 2013;97(6):717-725
9. Jerez *et al*., Blood 2012;119(25):6109-6118
10. Trobaugh-Lotrario *et al*., Bone Marrow Transplantation 2005;35(2):143-149
11. Grimwade D, *et al*. Br J Haematol. 2010; (3):17.
12. Seifert H, *et al*. Leukemia. 2009;23(4):656–63
13. Hernández *et al*., Haematologica 2000;85(5):481–5.
14. Moreno-Miralles *et al*., J Biol Chem 2005;280(48):40097-103
15. Reikvam H, *et al*. J Biomed Biotechnol. 2011; 2011:104631.
16. Grimwade *et al*., Blood 2001;98(5):1312-1320
17. Harrison *et al*., Journal of Clinical Oncology 2010;28(16):2674-2681
18. Březinová *et al*., 2005:160(2):188-192
19. Bench *et al*., Oncogene 2000;19(34):3902-13
20. Liu *et al*., Cancer Genet Cytogenet. 2006 Nov;171(1):9-16

Cytocell
an OGT company
aquarius



Haematopathology

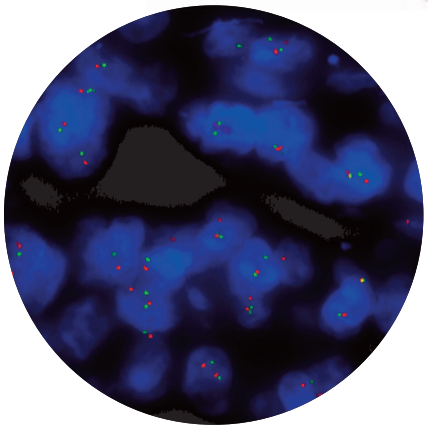
Contents

Haematopathology

The assessment of genetic changes in tissue biopsies can provide important information for prediction of tumour progression. The majority of these changes are either amplifications, deletions or other chromosomal rearrangements that can be detected using FISH.

Current methodologies, namely immunohistochemistry or blotting techniques, can provide information at the gene expression level but, when carried out on tissue sections (either cryostat or paraffin embedded), FISH can provide information at the DNA level, *in situ*, at the precise site within the tumour. This can reveal cell-to-cell heterogeneity and enable the detection of small clones of genetically distinct cells. This analysis can be made even more efficient through the use of automated image analysis systems and software.

BCL2 Breakapart



The BCL2 (*B-cell CLL/lymphoma 2*) gene located at 18q21.33 encodes one member of a large protein of a large protein family that regulates and contributes to programmed cell death, or apoptosis, by controlling mitochondrial membrane permeability[1].

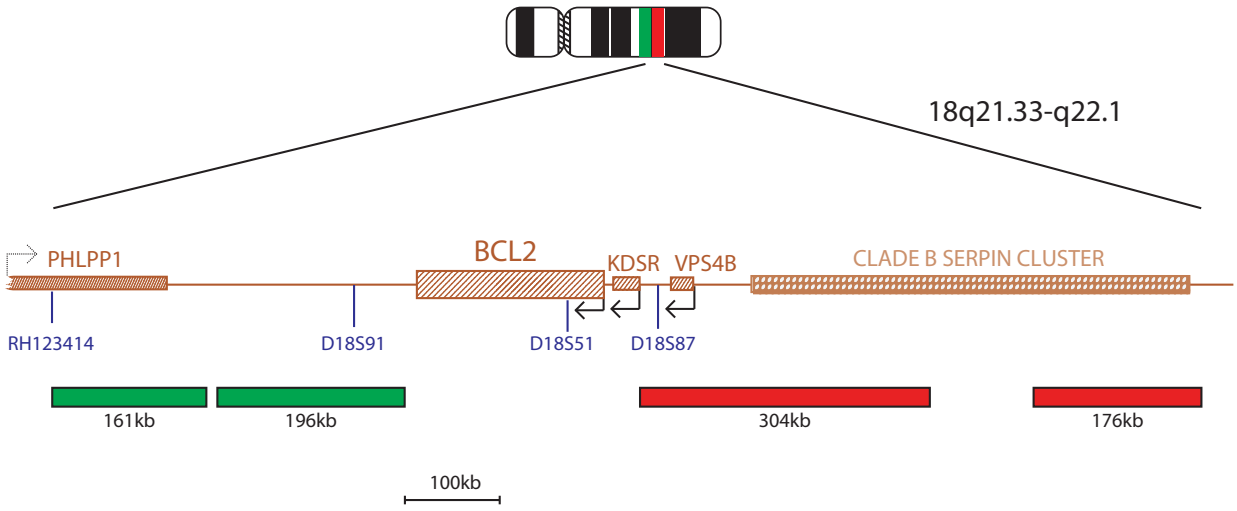
Translocations of the BCL2 gene result in constant expression of the BCL2 protein; these most frequently involve the immunoglobulin (IG) heavy chain (IGH) gene via a t(14;18)(q32.33;q21.33) translocation or, more rarely, involve the IG light chain (IGK or IGL) loci via t(2;18)(p11.2;q21.33) or t(18;22)(q21.33;q11.2) translocations[2].

The t(14;18)(q32.33;q21.33) translocation is thought to be brought about by an error in the joining function of the IGH gene, mediated by the observation that both IGH and BCL2 are arranged next to each other in 3D space in normal B lymphocytes[3]. The translocation breakpoint at the end of the Joining (J) segment, and the subsequent fusion of the BCL2 gene to this region, results in the BCL2 gene coming under the regulatory control of those processes normally involved in maintenance of IGH gene activity[4].

The t(14;18)(q32.33;q21.33) translocation is observed in 70-95% of follicular lymphoma (FL) cases and 20-30% of diffuse large B-cell lymphoma (DLBCL)[2]. Presence of the t(14;18) translocation in DLBCL is a predictor of outcome and has a poor prognostic effect[5]. BCL2 translocations have also been implicated in chronic B-cell lymphoproliferative disease (CLPD) and also occur occasionally in chronic lymphocytic leukaemia (CLL)[6].

REFERENCES

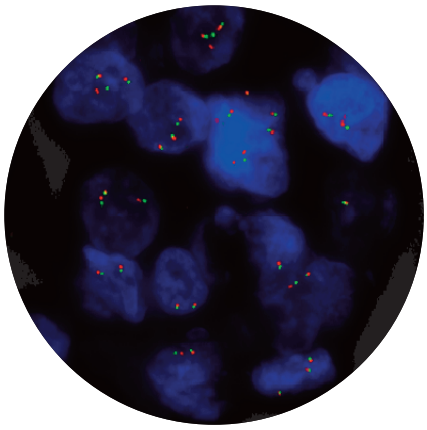
1. Sharpe *et al*., Biochim Biophys Acta. 2004;1644(2-3):107-13
2. Tomita N., J Clin Exp Hematop 2011;51(1):7-12
3. Roix *et al*., Nat Genet 2003;34(3):287-91
4. Stoos-Veić *et al*., Coll Antropol. 2010 Jun;34(2):425-9
5. Barrans *et al*., Clin Cancer Res 2003; 9; 2133
6. Bassegio L *et al*., Br J Haematol 2012;158(4):489-98



Cytocell an OGT company aquarius

Cat. No. **LPS 029-S** (5 tests)
Cat. No. **LPS 029** (10 tests)

BCL6 Breakapart*



Chromosomal rearrangements involving the BCL6 (*B-cell CLL/lymphoma 6*) gene at 3q27 are recognised recurrent abnormalities commonly seen in patients with B-cell malignancy[1].

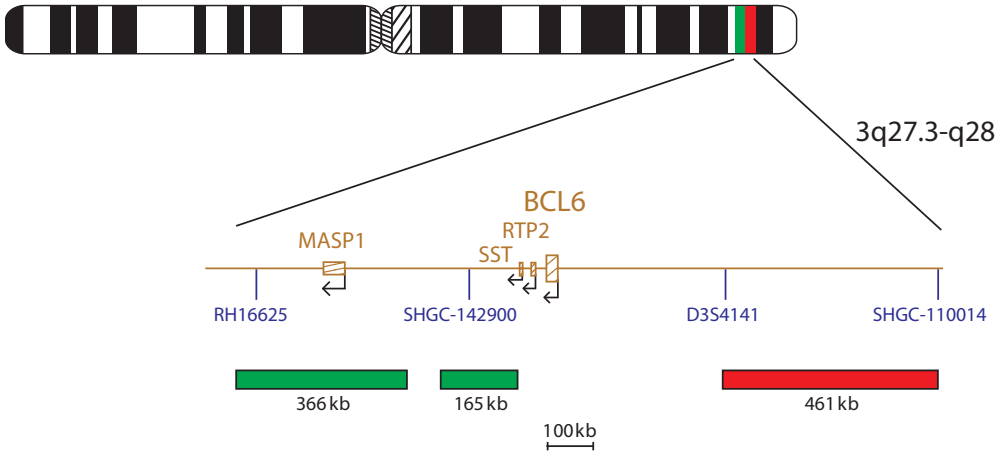
BCL6 rearrangements are the most common chromosomal abnormalities seen in diffuse large B-cell lymphoma (DLBCL), occurring in up to 35% of cases[2]. They are also seen frequently in follicular lymphoma, where they occur in up to 15% of cases[3]. BCL6 is expressed in normal germinal centre B-cells and follicle helper T-cells. BCL6 translocations alter expression by promoter substitution and cause deregulated expression of normal BCL6 protein[1,4].

Approximately 50% of BCL6 translocations will involve one of the three immunoglobulin loci (IGH, IGL or IGK); the remainder of translocations involve one of more than twenty different non-immunoglobulin genes[5]. Additionally, gains and amplifications of the BCL6 gene have also been reported in cases of B-cell lymphoma[6].

The presence of concurrent BCL6 rearrangements with MYC and/or BCL2 rearrangements in patients with 'dual-hit' lymphoma has been shown to be associated with aggressive disease[7].

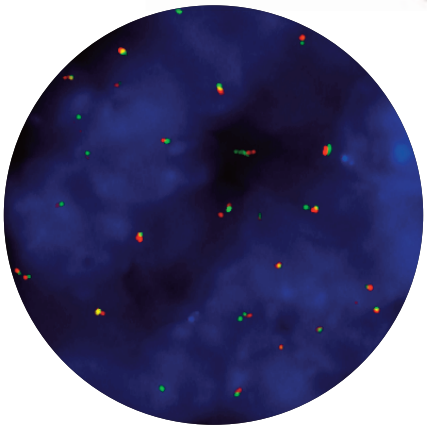
REFERENCES

1. Wagner SD, *et al*. Br J Haematol. 2011 Jan;152(1):3-12
2. Lossos I, *et al*. Leukemia. 2003; 17(7): 1390-7
3. Akasaka T, *et al*.. Blood. 2003;102(4):1443-8
4. Ye BH, *et al*. EMBO J 1995 Dec 15;14(24):6209-17
5. Ohno H. J Clin Exp Hematop 2006 Nov;46(2):43-53
6. Karube K, *et al*. Mod Pathol 2008;21(8):973-8
7. Aukema SM, *et al*. Blood. 2011; Feb 24;117(8):2319-31



***A similar product is also available in the Haematology range, refer to page 21.**

CCND1 Breakapart



Rearrangements involving the CCND1 (*cyclin D1*) region at 11q13.3 are seen in a variety of tumour types.

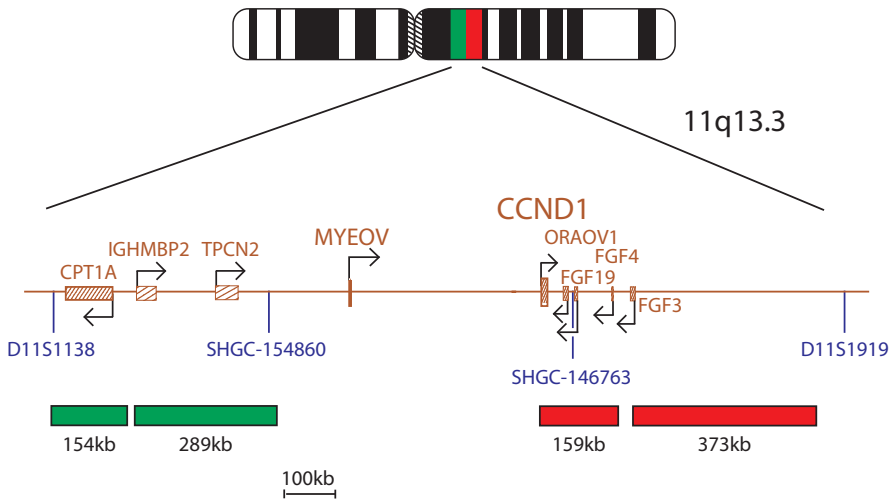
The t(11;14)(q13;q32) rearrangement involving CCND1 and IGH is considered the hallmark of mantle cell lymphoma (MCL)[1], the presence of which can be used to aid in the differential diagnosis of CD5+ B-cell lymphoproliferative disorders[2].

A similar t(11;14) translocation is also seen in 15% patients with multiple myeloma[3,4], where it appears to be associated with a favourable outcome in most series and is regarded as neutral with regard to prognosis[5].

Amplification of the CCND1 region has been reported in a number of solid tumours including breast cancer[6], squamous cell carcinoma[7] and gastric cancer[8].

REFERENCES

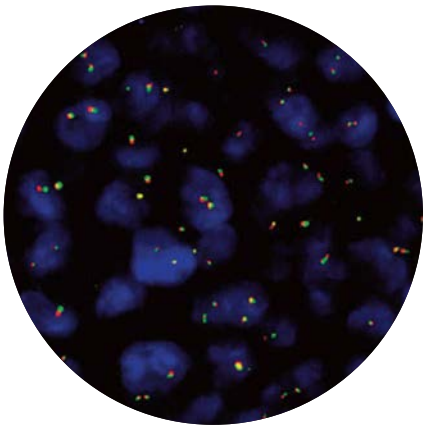
1. Vose JM. Am J Hematol. 2013;88(12):1082-8
2. Ho AK, *et al*.. Am J Clin Pathol 2009;131:27-32
3. Sawyer JR. Cancer Genet. 2011 Jan;204(1):3-12
4. Palumbo A *et al*. J Clin Oncol 2015;33:2863-9
5. Chng *et al*. Best Pract Res Clin Haematol 2007;20:571-96
6. Roy PG *et al*. Int J Cancer [Internet] 2010;127:355-60
7. Mahdey HM, *et al*. Asian Pac J Cancer Prev 2011;12:2199-204
8. Stahl P, *et al*. BMC Gastroenterol 2015;15:7



Cytocell an OGT company aquarius

Cat. No. **LPS 032-S** (5 tests)
Cat. No. **LPS 032** (10 tests)

IGH Breakapart*



Recurrent rearrangements involving the IGH (*immunoglobulin heavy locus*) gene at 14q32.33 with a wide range of partner genes are seen in lymphomas and haematological malignancies[1].

A t(8;14)(q24;q32) translocation, involving IGH and the MYC gene at 8q24, is frequently seen in Burkitt lymphoma[2] and diffuse large B-cell lymphoma (DLBCL)[3]. Other rearrangements frequently reported in B-cell lymphoma include: the t(14;18)(q32;q21) translocation, involving IGH and the BCL2 gene, seen in both follicular lymphoma and DLBCL[4]; and the t(11;14)(q13;q32) involving IGH and the CCND1 gene, which is the hallmark of mantle cell lymphoma (MCL)[5].

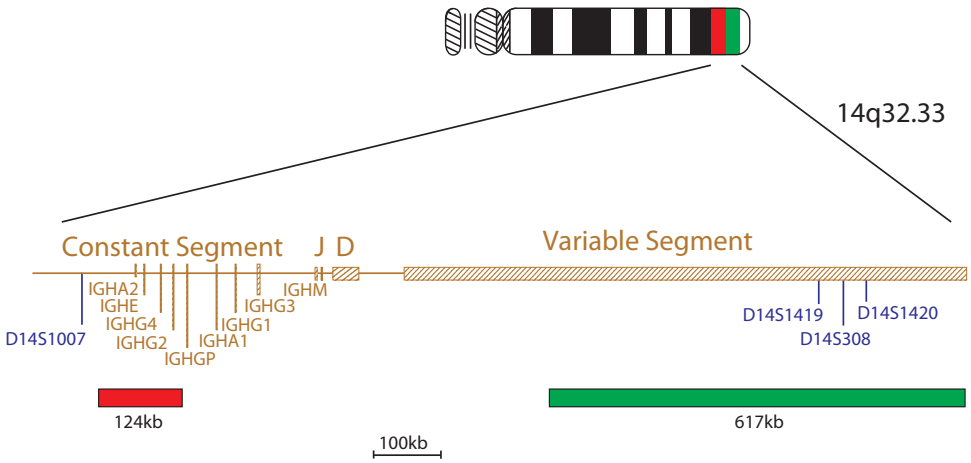
IGH rearrangements with a number of different gene partners are a frequent finding in patients with multiple myeloma, including: t(4;14)(p16;q32) translocations involving IGH with FGFR3 and WHSC1; t(6;14)(p21;q32) translocations involving IGH and CCND3; t(11;14)(q13;q32) translocations involving IGH and CCND1; t(14;16)(q32;q23) translocations involving IGH and MAF, and t(14;20)(q32;q12) translocations involving IGH and MAFB[6,7].

IGH rearrangements are also reported as recurrent abnormalities in patients with lymphoplasmacytic lymphoma (LPL), chronic lymphocytic leukaemia (CLL), extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT) type and acute lymphoblastic leukaemia (ALL)[8].

The breakapart design for this probe set allows the detection of rearrangements of the IGH region, regardless of partner gene or chromosome involved.

REFERENCES

1. Gozzetti A, *et al*. Cancer Res.2002 Oct 1;62(19):5523-7
2. Ferry JA. Oncologist 2006 Apr;11(4):375-83
3. Li S, *et al*. Mod Pathol. 2012 Jan;25(1):145-56
4. Snuderl M, *et al*. Am J Surg Pathol. 2010 Mar;34(3):327-40
5. Vose JM. Am J Hematol. 2013;88(12):1082-8
6. Bergsagel PL, *et al*. Proc Natl Acad Sci USA. 1996 Nov 26;93(24):13931-6
7. Sawyer JR. Cancer Genet. 2011 Jan;204(1):3-12
8. Swerdlow SH, *et al*, eds. 2008 WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC



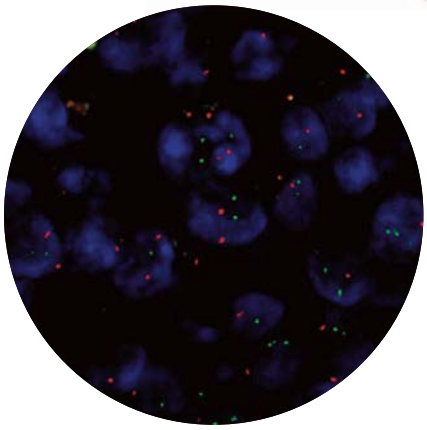
***Similar products are available in the Haematology range, refer to pages 41 and 42.**

Cytocell an OGT company aquarius

Cat. No. **LPS 033-S** (5 tests)

Cat. No. **LPS 033** (10 tests)

IGH/BCL2 Translocation, Dual Fusion*

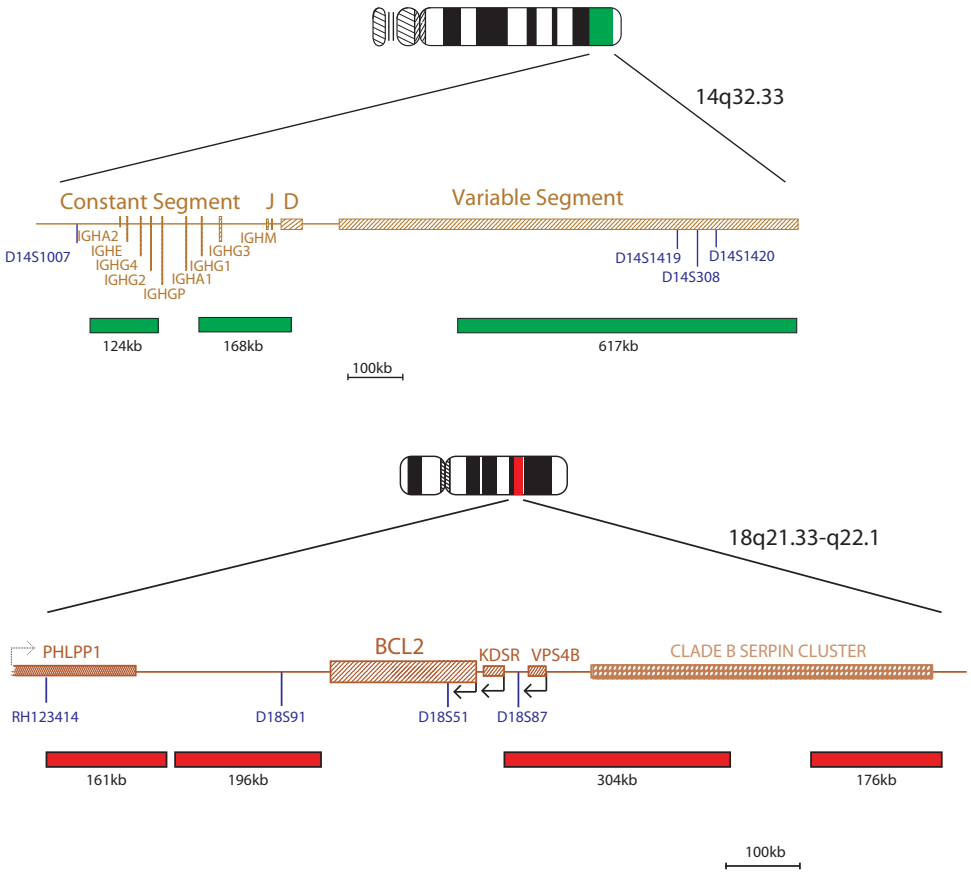


The t(14;18)(q32;q21) translocation involving the IGH (*immunoglobulin heavy locus*) gene at 14q32.33 and the BCL2 (*B-cell CLL/lymphoma 2*) gene at 18q21.33 is a recognised recurrent abnormality seen in B-cell malignancies.

IGH-BCL2 rearrangements are observed in 70-95% of follicular lymphoma (FL) cases and 20-30% of diffuse large B-cell lymphoma (DLBCL)[1]. Presence of the t(14;18) translocation in DLBCL is a predictor of outcome and has a poor prognostic effect[2]. BCL2 translocations have also been implicated in chronic B-cell lymphoproliferative disease (CLPD) and also occur occasionally in chronic lymphocytic leukaemia (CLL)[3].

REFERENCES

1. Tomita N., J Clin Exp Hematop 2011;51(1):7-12
2. Barrans *et al.*, Clin Cancer Res 2003; 9; 2133
3. Bassegio L *et al.*, Br J Haematol 2012;158(4):489-98



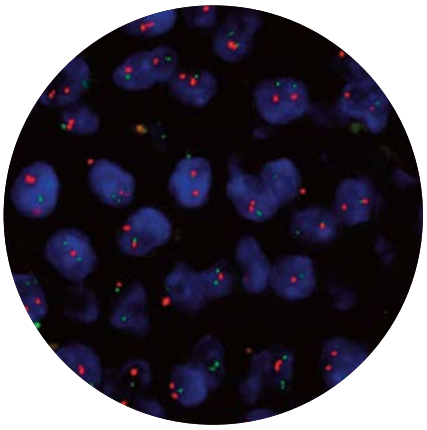
*** A similar product is also available within the Haematology range, refer to page 43.**

Cytocell an OGT company aquarius

Cat. No. **LPS 031-S** (5 tests)

Cat. No. **LPS 031** (10 tests)

IGH/CCND1 Translocation, Dual Fusion*



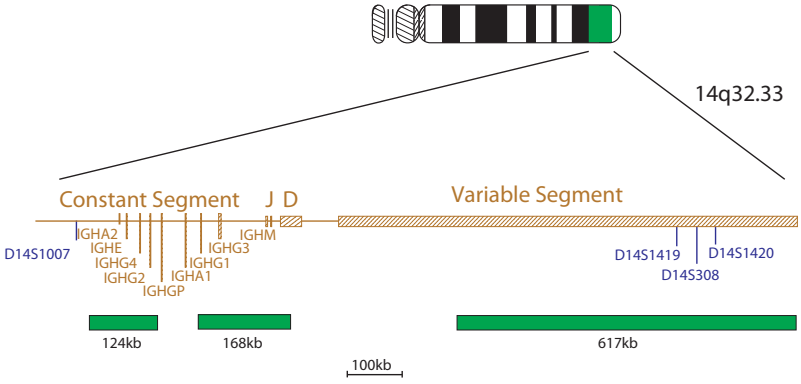
The t(11;14)(q13;q32) translocation involving CCND1 (*cyclin D1*) gene at 11q13.3 and the IGH (*immunoglobulin heavy locus*) gene at 14q32 is associated with mantle cell lymphoma.

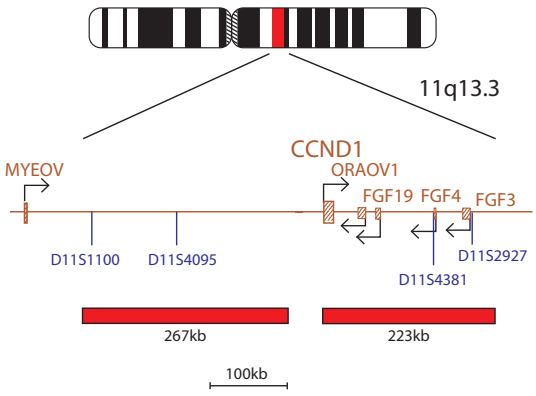
The t(11;14)(q13;q32) rearrangement involving CCND1 and IGH is considered the hallmark of mantle cell lymphoma (MCL)[1], the presence of which can be used to aid in the differential diagnosis of CD5+ B-cell lymphoproliferative disorders[2].

Amplification of the CCND1 region has been reported in a number of solid tumours including breast cancer[3], squamous cell carcinoma[4] and gastric cancer[5].

REFERENCES

1. Vose JM. Am J Hematol. 2013;88(12):1082-8
2. Ho AK, *et al*.. Am J Clin Pathol 2009;131:27-32
3. Roy PG *et al*. Int J Cancer [Internet] 2010;127:355-60
4. Mahdey HM, *et al*. Asian Pac J Cancer Prev 2011;12:2199-204
5. Stahl P, *et al*. BMC Gastroenterol 2015;15:7



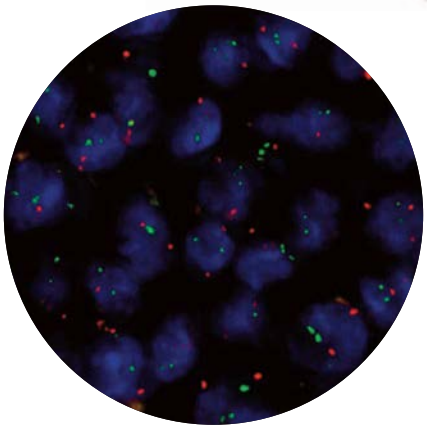


*** A similar product is also available within the Haematology range, refer to page 44.**

Cytocell an OGT company aquarius

Cat. No. **LPS 034-S** (5 tests)
Cat. No. **LPS 034** (10 tests)

IGH/MALT1 Translocation, Dual Fusion



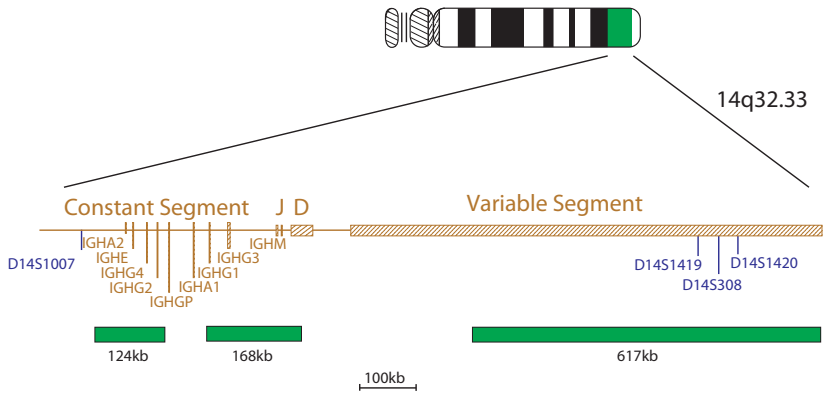
The t(14;18)(q32;q21) translocation involving the IGH (*immunoglobulin heavy locus*) gene at 14q32 and the MALT1 (*MALT1 paracaspase*) at 18q21 is a recognised recurrent abnormality seen in MALT lymphoma[1].

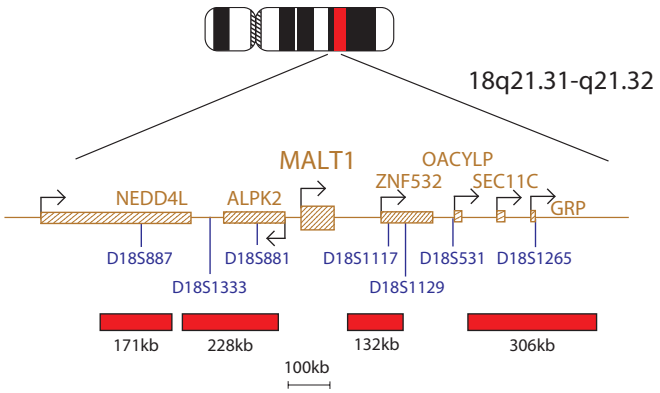
Rearrangements of MALT1 are associated with extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT) type and are characterised by two main translocations: the t(11;18)(q21;q21.32) involving the BIRC3 gene and the t(14;18)(q32;q21.32) involving the IGH gene. Other MALT1-associated translocations are rare[1,3].

The t(14;18) translocation is present in approximately 18% of MALT lymphomas and is most frequently found in liver, skin and ocular adnexa sites rare for the t(11;18)[2]. Both translocations result in the constitutive activation of the NF-kappaB pathway[4].

REFERENCES

1. Murga Penas EM *et al*., Blood 2010;115(11):2214-9
2. Streubel B *et al*., Blood 2003;101:2335-2339
3. Remstein ED *et al*., Am J Pathol 2000;156:1183-1188
4. Lucas PC *et al*., J Biol Chem 2001;276(22):19012-9

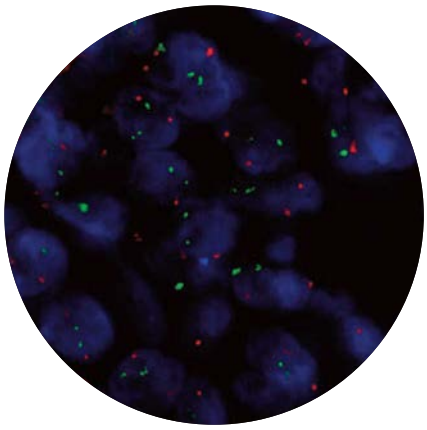




Cytocell an OGT company aquarius

Cat. No. **LPS 035-S** (5 tests)
Cat. No. **LPS 035** (10 tests)

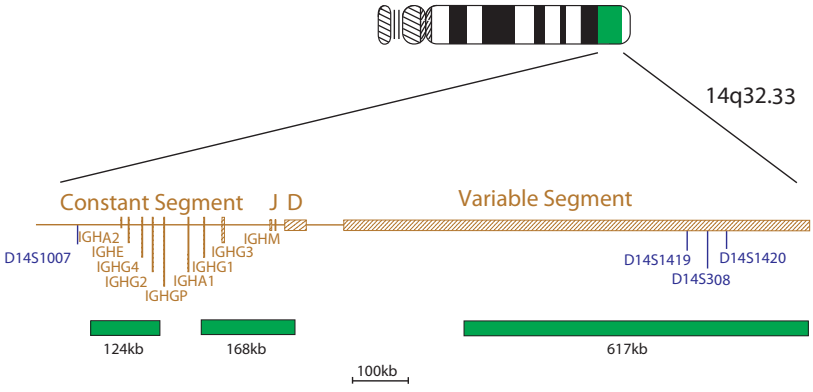
IGH/MYC Translocation, Dual Fusion*

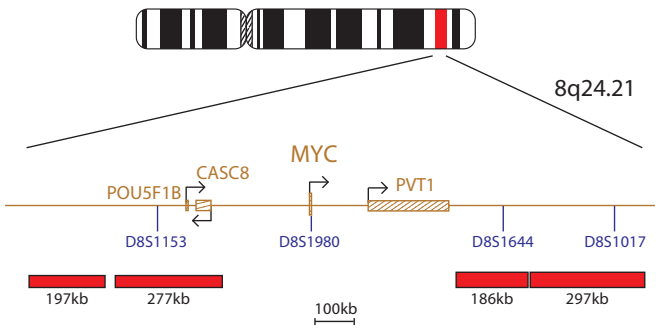


The t(8;14)(q24;q32) translocation involving the IGH (*immunoglobulin heavy locus*) gene at 14q32 and the MYC (*v-myc avian myelocytomatosis viral oncogene homolog*) oncogene at 8q24 is a recognised recurrent abnormality commonly seen in patients with B-cell malignancy.

IGH-MYC rearrangements are detected in up to 85% of cases of Burkitt lymphoma at diagnosis[1]. They are also seen in diffuse large B-cell lymphoma (DLBCL)[2], multiple myeloma and plasmablastic lymphoma[3,4].

In an IGH-MYC rearrangement the translocation breakpoints on chromosome 14 are clustered to a narrow region 5' to the intron enhancer of the immunoglobulin heavy chain, whereas the breakpoints on chromosome 8 can occur more than 340kb upstream of MYC, with no preferential site[5]. The translocation brings MYC into close proximity to the IGH enhancer and results in the up-regulation of MYC. Over-expression of the transcription factor stimulates gene amplification, resulting in uncontrolled cell proliferation[6].





REFERENCES

1. Perkins AS, Friedberg JW. Hematology Am Soc Hematol Educ Program. 2008;341-8
2. Ott G, *et al*. Blood. 2013 Dec 5;122(24):3884-91
3. Walker BA, *et al*. Blood Cancer J. 2014;4(3)
4. Elyamany G, *et al*. Adv Hematol 2015;2015:315289
5. Joos *et al*., Human Molecular Genetics 1992;1(8):625-32
6. Erikson J *et al*., Proc Natl Acad Sci USA 1983;80(3):820-4

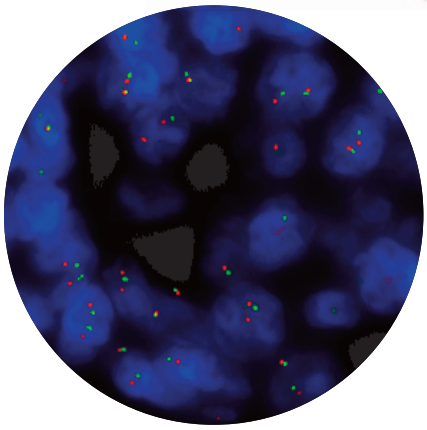
*** A similar product is also available within the Haematology range, refer to page 46.**

IGK Breakapart and IGL Breakapart*

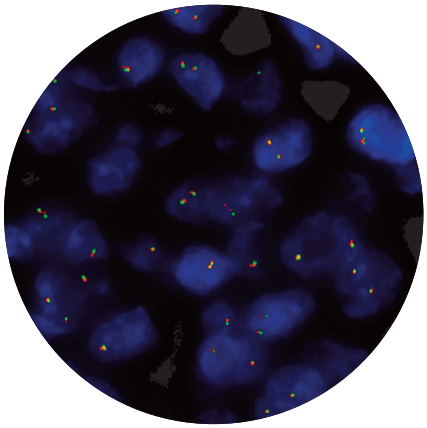
Recurrent rearrangements involving the IGK (*immunoglobulin kappa locus*) gene at 2p11.2 or the IGL (*immunoglobulin lambda locus*) gene at 22q11, with a wide range of partner genes, are seen in lymphomas and haematological malignancies.

A large number of B-cell malignancies harbour translocations involving the immunoglobulin (IG) loci. The majority of cases will show rearrangements involving the IGH gene; however, variant translocations have been described in 5-10% of B-cell neoplasms which involve either the immunoglobulin kappa (IGK) light chain locus at 2p11.2 or the immunoglobulin lambda (IGL) light chain locus at 22q11[1,2].

Variant translocations involving the IG light chain loci are seen in Burkitt lymphoma and multiple myeloma, with the presence of a t(2;8)(p12;q24) MYC-IGK, or t(8;22)(q24;q11) MYC-IGL[3,5]. In diffuse large B-cell lymphoma (DLBCL), translocations may involve the BCL6 gene via t(2;3)(p12;q27) or t(3;22)(q27;q11) translocations, or the BCL2 gene via t(2;18)(p12;q21) or t(18;22)(q21;q11) translocations[6].



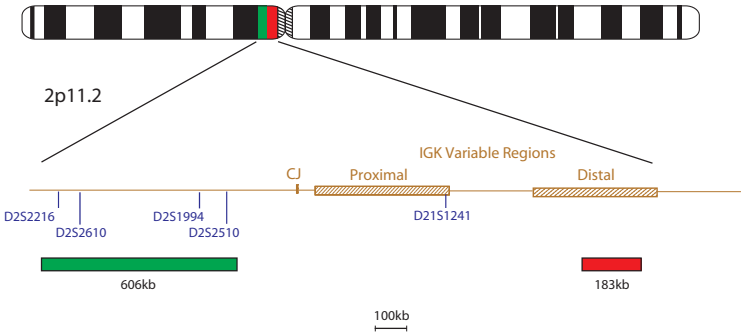
IGK Breakapart



IGL Breakapart

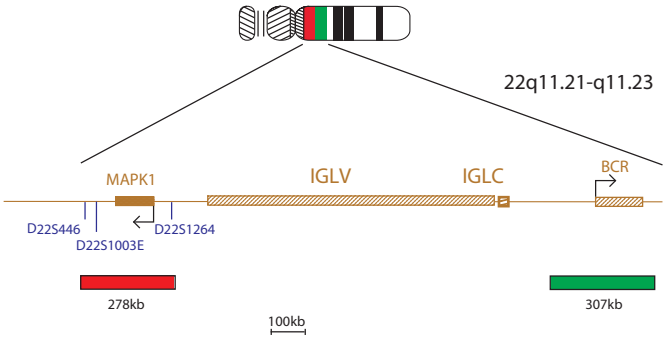
IGK Breakapart

Cat. No. **LPS 038**



IGL Breakapart

Cat. No. **LPS 039**



REFERENCES

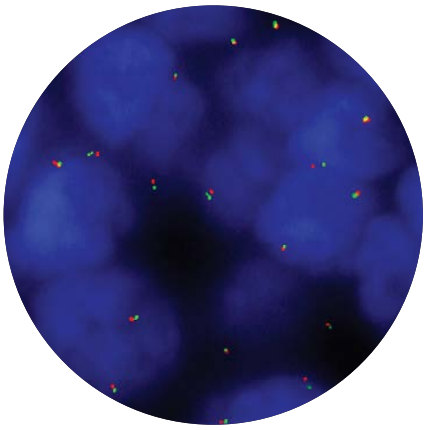
1. Poulseu TS *et al*., Leukemia 2002;16:2148-55
2. Martin-Subero JI *et al*., Int J Cancer 2002;98:470-4
3. Kornblau SM *et al*., Hematol Oncol 1991;9:63-78
4. Walker BA, *et al*. Blood Cancer J; 2014;4(3):e191
5. Chaganti SR *et al*., Genes Chromosomes Cancer 1998;23:323-7
6. Tashiro S *et al*., Oncogene 1992;7:573-7

*** Similar products are also available within the Haematology range, refer to page 51.**

Cytocell an OGT company aquarius

Cat. No. **LPS 017-S** (5 tests)
Cat. No. **LPS 017** (10 tests)

MALT1 Breakapart



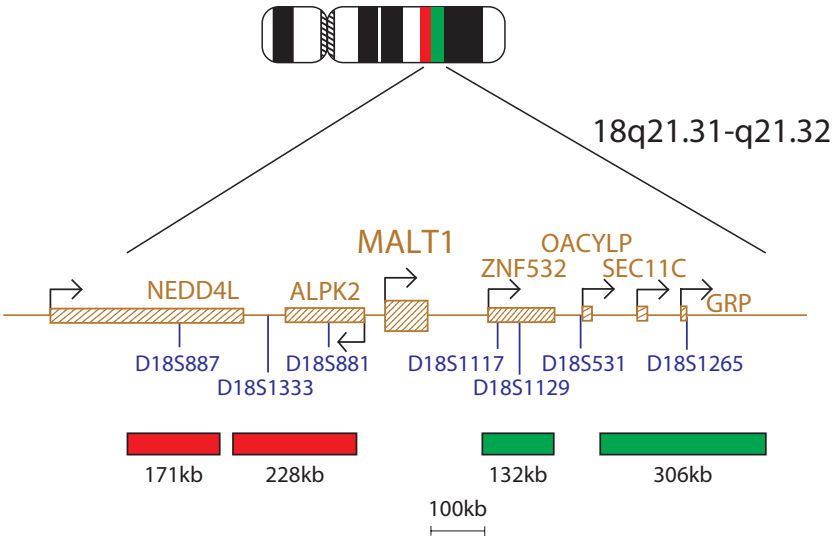
The MALT1 (*MALT1 paracaspase*) gene is located at 18q21.

Rearrangements of MALT1 are associated with extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT) type and are characterised by two main translocations: the t(11;18)(q21;q21.32) involving the BIRC3 gene and the t(14;18)(q32;q21.32) involving the IGH (*immunoglobulin heavy locus*) gene. Other MALT1-associated translocations are rare[1].

The t(11;18) translocation is present in 18-33% of cases of MALT lymphoma and is most frequently found in pulmonary, gastrointestinal and parotid gland MALT1 lymphomas[1,2,3]; the t(14;18) translocation is present in approximately 18% of MALT lymphomas and is most frequently found in liver, skin, and ocular adnexa - sites rare for the t(11;18)[3]. Both translocations result in the constitutive activation of the NF-kappaB pathway[4].

REFERENCES

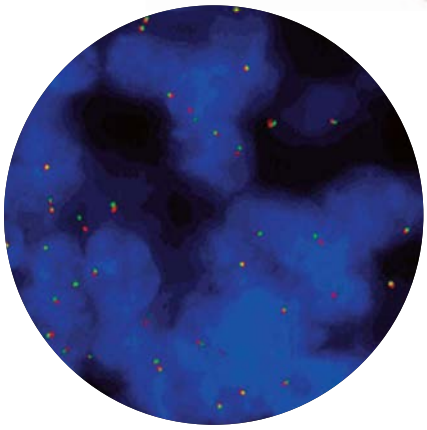
1. Murga Penas EM *et al*., Blood 2010;115(11):2214-9
2. Auer IA *et al*., Ann Oncol 1997;8(10):979-85
3. Streubel B *et al*., Blood 2003;101(6):2335-9
4. Lucas PC *et al*., J Biol Chem 2001;276(22):19012-9



Cytocell an OGT company aquarius

Cat. No. **LPS 027-S** (5 tests)
Cat. No. **LPS 027** (10 tests)

MYC Breakapart*

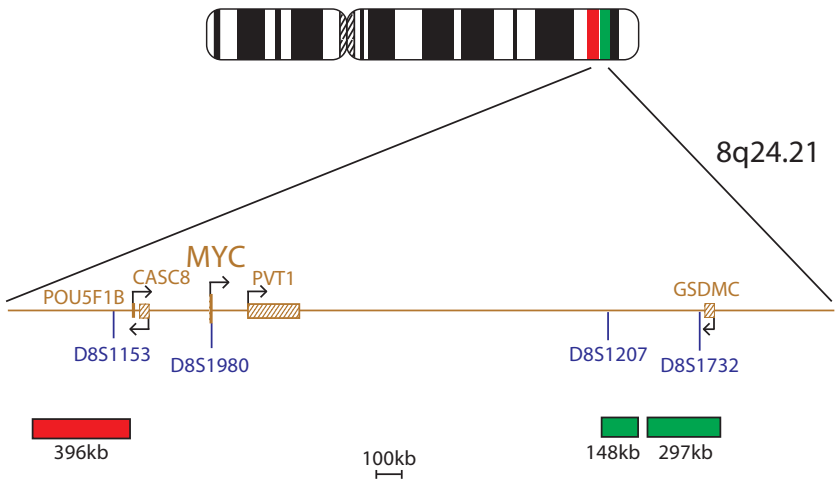


Chromosomal rearrangements involving the MYC (*v-myc avian myelocytomatosis viral oncogene homolog*) gene at 8q24 are recognised recurrent abnormalities commonly seen in patients with B-cell malignancy.

MYC rearrangements, activating MYC by translocation with one of the three immunoglobulin loci (IGH, IGL or IGK), are detected in almost all cases of Burkitt lymphoma at diagnosis[1]. They are also seen in diffuse large B-cell lymphoma (DLBCL)[2] , multiple myeloma and plasmablastic lymphomas[3,4], amongst other diseases.

MYC has also been shown on rare occasions to be involved in rearrangements with a number of non-immunoglobulin partners[5].

The presence of concurrent MYC rearrangements with BCL2 and/or BCL6 rearrangements in patients with 'dual-hit' lymphoma has been shown to be associated with aggressive disease[6].



REFERENCES

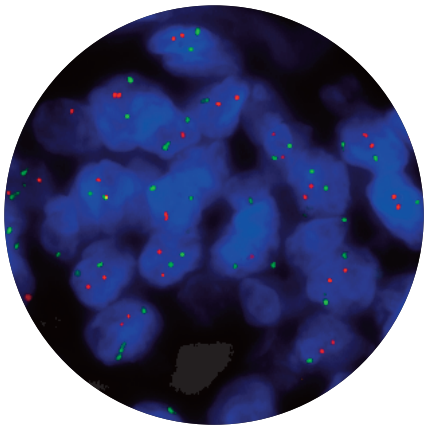
1. Perkins AS, Friedberg JW. Hematology Am Soc Hematol Educ Program. 2008;341-8
2. Ott G, et al. Blood. 2013 Dec 5;122(24):3884-91
3. Walker BA, et al. Blood Cancer J. 2014;4(3)
4. Elyamany G, et al. Adv Hematol 2015;2015:315289
5. Bertrand P, et al. Leukemia 2007;21:515-23
6. Aukema SM, et al. Blood. 2011; Feb 24;117(8):2319-31

*** A similar product is also available within the Haematology range, refer to page 28.**

Cytocell an OGT company aquarius

Cat. No. **LPS 036-S** (5 tests)
Cat. No. **LPS 036** (10 tests)

P16 (CDKN2A) Deletion*



The CDKN2A (*cyclin-dependent kinase inhibitor 2A*) gene at 9p21 is a tumour suppressor gene that has been shown to be deleted in wide range of human malignancies.

Loss of the CDKN2A gene results in cellular proliferation and dysregulation of pro-apoptotic pathways. There are two proteins produced by the CDKN2A gene: $p16^{INK4a}$ and $p14^{ARF}$; these protein products have been linked to two tumour suppressor pathways – the RB pathway and the p53 pathway, respectively[1].

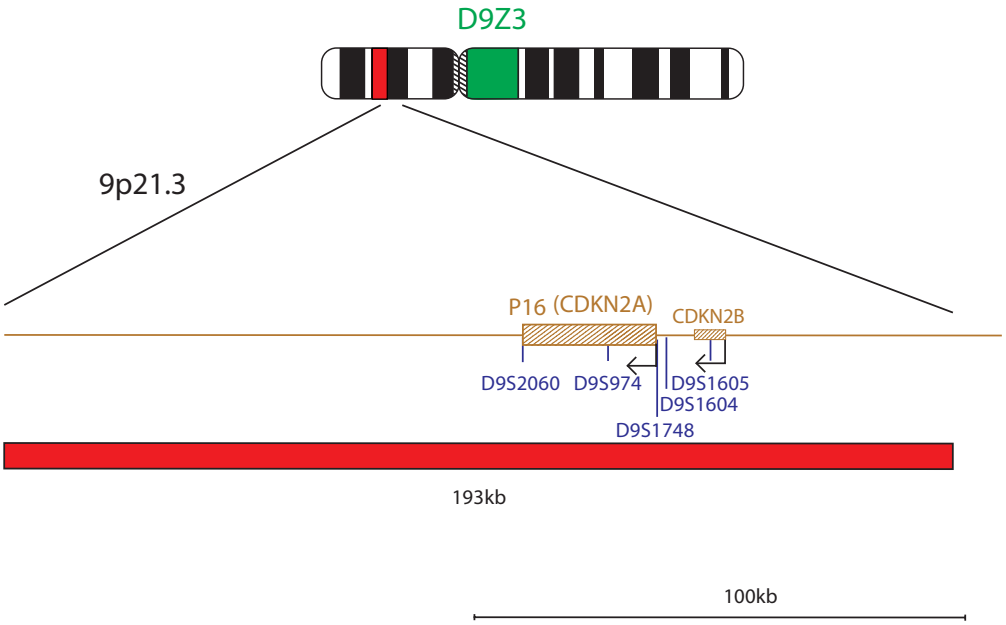
Deletions of 9p that include the CDKN2A gene are frequently reported in patients with acute lymphoblastic leukaemia (ALL): in approximately 30% of adult B-cell ALLs, 30% of childhood ALLs and up to 50% of T-cell ALLs. In adult B-cell ALL, CDKN2A deletions are frequently acquired in disease progression[2,3,4,5].

Deletions including the CDKN2A locus have been reported in up to a third of patients with diffuse large B-cell lymphoma (DLBCL)[6] and, in glioma, CDKN2A loss has been implicated with shorter overall survival in WHO grade I-III astrocytomas[7].

Losses of the CDKN2A region have also been reported in malignant mesothelioma, melanoma, and bladder cancer[8,9,10].

REFERENCES

1. Møller MB, *et al*. Leukemia. 1999 Mar;13(3):453-9
2. Moorman A V, *et al*. Blood. 2007;109(8):3189-97
3. Sulong S, *et al*. Blood. 2014;113(1):100-7
4. Schwab CJ, *et al*. Haematologica .2013 Jul;98(7):1081-8
5. Xu N, *et al*. J Cancer. 2015;6(11):1114-20
6. Jardin F, *et al*., Blood. 2010;116(7):1092-104
7. Reis GF, *et al*. J Neuropathol Exp Neurol. 2015 May;74(5):442-52
8. Conway C, *et al*. Genes Chromosomes Cancer. 2010 May;49(5):425-38
9. Relan V, *et al*. PLoS One. 2013;8(3):e58132
10. Stadler WM, *et al*. Clin Cancer Res. 2001;7(6):1676-82



*** A similar product is also available within the Haematology range, refer to page 57.**

P53 (TP53) Deletion*

The TP53 (*tumor protein p53*) gene at 17p13.1 is a tumour-suppressor gene that has been shown to be deleted in a wide range of human malignancies.

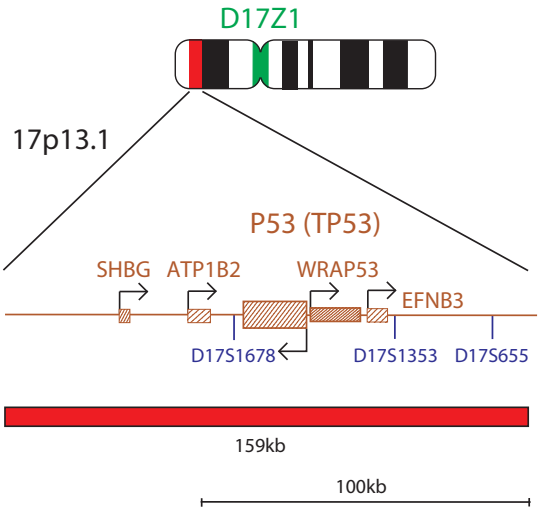
The TP53 gene is one of most important tumour suppressor genes; it acts as a potent transcription factor with a fundamental role in the maintenance of genetic stability. Screening for TP53 loss is important as deletions or losses of the short arm of chromosome 17, which includes the TP53 region, are reported in many cancers and are often associated with disease progression, inferior response to treatment and/or a poor prognosis[1-9].

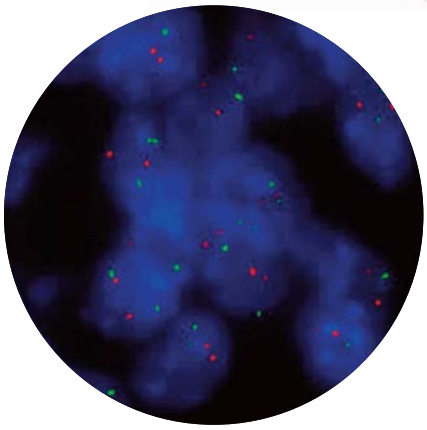
In particular, loss of TP53 is reported in 10% of patients with chronic lymphocytic leukaemia (CLL), and is considered to be the poorest prognostic marker in that disease[1,2]. In acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL), TP53 loss is associated with a poor outcome and is often seen as a marker of disease progression or secondary disease. [3-5]

TP53 loss in patients with multiple myeloma is a late event, where it is seen as a marker of disease progression and is associated with a very poor prognosis[6,7].

In non-Hodgkin lymphoma, TP53 losses are reported in diffuse large B-cell lymphoma (DLBCL) often as part of 'dual-hit' lymphoma or plasmablastic phenotypes.[8] In mantle cell lymphoma (MCL), TP53 losses are associated with a poor outcome, and with a dismal outcome when seen with concurrent CDKN2A deletions.[9]

TP53 loss has also been reported in a wide range of solid tumour types including gastric cancer[9] breast cancer[10] and non-small cell lung cancer[11].





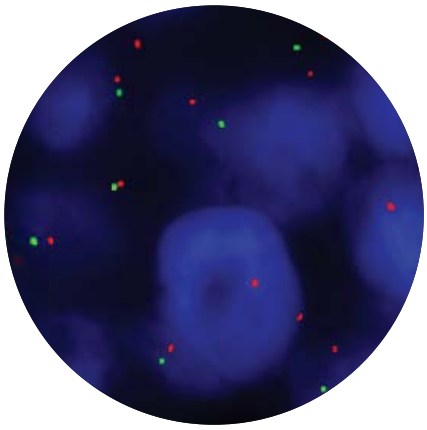
REFERENCES

1. Rossi D, *et al*. Blood. 2013 Feb 21;121(8):1403-12
2. Baliakas P, *et al*. Leukemia. 2014;(April):1-8
3. Grimwade D, *et al*. Br J Haematol. 2010; (3):17
4. Seifert H, *et al*. Leukemia. 2009;23(4):656-63
5. Stengel A, *et al*. Blood. 2014;124(2):251-8
6. Palumbo A, *et al*. J Clin Oncol. 2015 Sep 10;33(26):2863-9
7. Fonseca R, *et al*. Leukemia. 2009 Dec;23(12):2210-21
8. Simonitsch-Klupp I, *et al*. Leukemia. 2004 Jan;18(1):146-55
9. Khayat AS, *et al*. BMC Gastroenterol. 2009;9:55
10. Liu JC, *et al*. EMBO Mol Med. 2014 Dec;6(12):1542-60
11. Mogi A, Kuwano H. J. Biomed Biotechnol. 2011;2011:583929

*** A similar product is also available within the Haematology range, refer to page 58.**

Cytocell an OGT company aquarius
Cat. No. **LPS 011-S** (5 tests)
Cat. No. **LPS 011** (10 tests)

RB1 Deletion



The RB1 (*retinoblastoma 1*) gene located at 13q14.2 is a tumour suppressor gene. Mutations or losses of the RB1 gene have been shown to cause retinoblastoma, an eye cancer that is seen in infants and small children[1].

Losses or mutations of the RB1 gene are also implicated secondary tumours, such as osteosarcoma or soft tissue sarcoma[2], arising in patients with retinoblastoma.

Deletions of 13q including the RB1 gene may also occur as a result of a progressional tumourigenic event in some leukaemias[3], as well as in some breast, lung, bladder, oesophagus and prostate cancers[4].

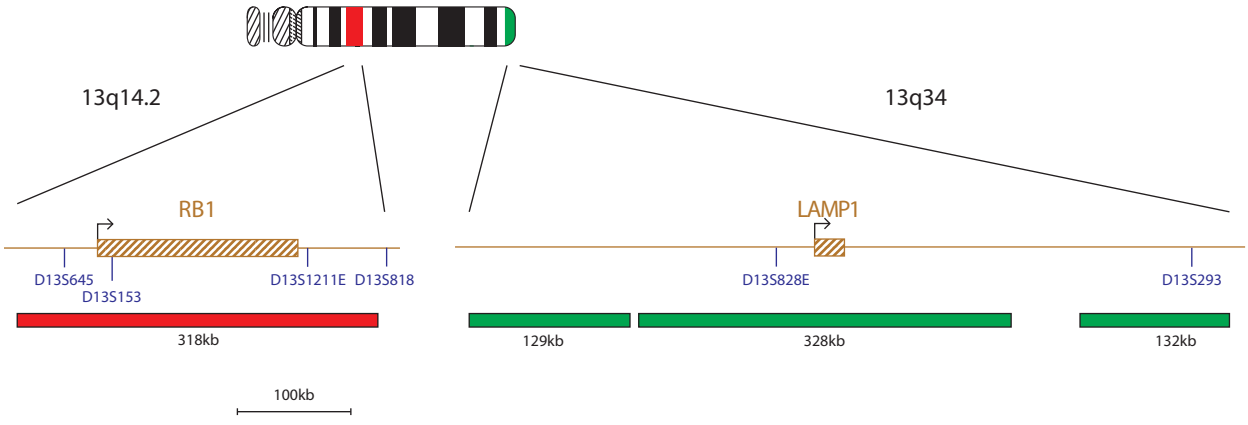
Heterogeneous interstitial deletions of the 13q14 region are the most common cytogenetic aberrations seen in patients with chronic lymphocytic leukaemia (CLL), seen in up to 60% of cases[5]. In approximately 20% of cases, these deletions will encompass the RB1 locus; these larger deletions have been associated with a shortened survival compared with patients that have smaller deletions that do not include the RB1 locus[6].

Chromosome 13 losses and larger deletions of the long arm of chromosome 13, encompassing the RB1 locus, are reported in approximately 50% of cases of multiple myeloma[7,8].

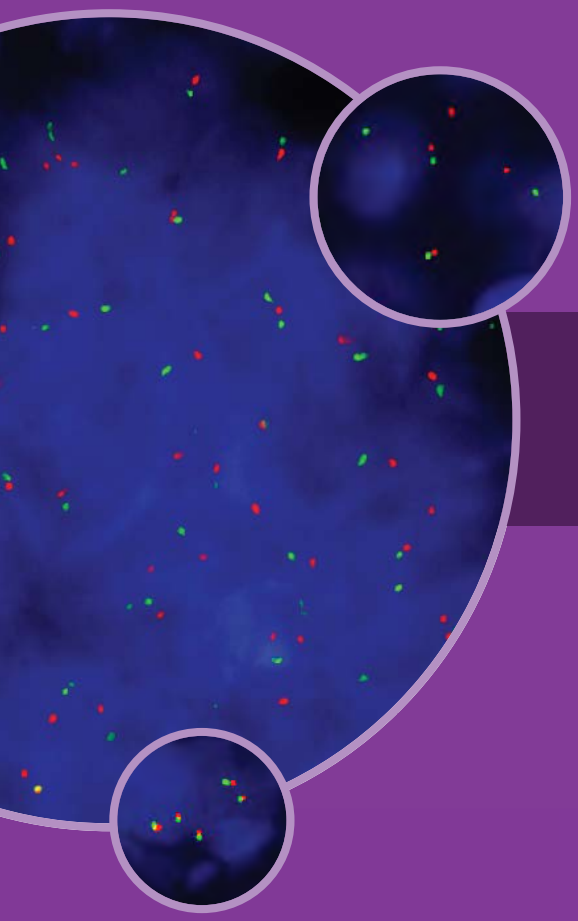
Deletions of the long arm of chromosome 13 that include the RB1 locus have also been reported in patients with myeloid neoplasia and acute lymphoblastic leukaemia[9,10].

REFERENCES

1. Rushlow D *et al*. The Lancet Oncology. 2013;14(4):327-334
2. Draper *et al*., Br J Cancer 1986;53:661-71 4
3. Juneau *et al*., Cancer Genet Cytogenet. 1998;103:117-23 5
4. Benedict *et al*., J. clin. Invest. 1990;85:988-993 (1990)
5. Rossi D, *et al*. Blood. 2013 Feb 21;121(8):1403-12
6. Ouillette P, *et al*. Clin Cancer Res. 2011;17(21):6778-90
7. Ross FM, *et al*. Haematologica. 2012 Aug;97(8):1272-7
8. Fonseca R, *et al*. Leukemia. 2001 Jun;15(6):981-6
9. Hosokawa K, *et al*. Haematologica. 2012;97(12):1845-9
10. Schneider NR, *et al*. Blood. 2000 Oct 1;96(7):2543-9



Cytocell
an OGT company
aquarius



Pathology

Contents

Pathology

The assessment of genetic changes in tissue biopsies can provide important information for prediction of tumour progression. The majority of these changes are either amplifications, deletions or other chromosomal rearrangements that can be detected using FISH.

Current methodologies, namely immunohistochemistry or blotting techniques, can provide information at the gene expression level but, when carried out on tissue sections (either cryostat or paraffin embedded), FISH can provide information at the DNA level, *in situ*, at the precise site within the tumour. This can reveal cell-to-cell heterogeneity and enable the detection of small clones of genetically distinct cells. This analysis can be made even more efficient through the use of automated image analysis systems and software.

Tissue Pretreatment Kit

Introducing the first pretreatment kit capable of preparing slides for CISH and/or FISH analysis on formalin-fixed, paraffin-embedded (FFPE) tissue.

Our ready-to-use Tissue Pretreatment Kit has been optimised to produce excellent visual results with our extensive Aquarius® Pathology FISH range.

To further extend the utility of the kit we have also validated its use with other commercially available CISH (chromogenic *in situ* hybridisation) and FISH (fluorescence in situ hybridisation) DNA probes*.

With ease-of-use and convenience in mind, our simple two stage FFPE slide preparation protocol employs the use of ready-to-use reagents, which have been optimised to increase the permeabilisation of cell membranes and facilitate penetration of the desired FISH or CISH DNA probe.

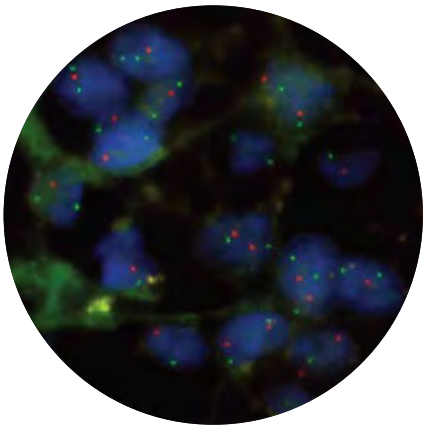
Product Information	Kit Components
Aquarius® Tissue Pretreatment Kit**	Reagent 1 (1x1L) Reagent 2 (1x10mL)

*A list of manufacturers is available upon request.
**This product is provided under an agreement between Life Technologies Corporation and Cytocell Ltd and is available for human diagnostics or life science use only.

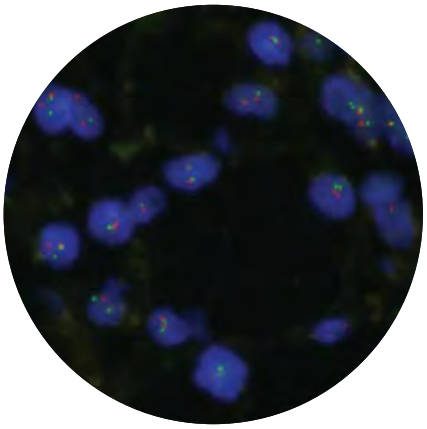
Cytocell an OGT company aquarius

Cat. No. **LPS 047-S** (5 tests)
Cat. No. **LPS 047** (10 tests)

1p36/1q25 and 19q13/19p13 Deletion Probe Kit



1p36



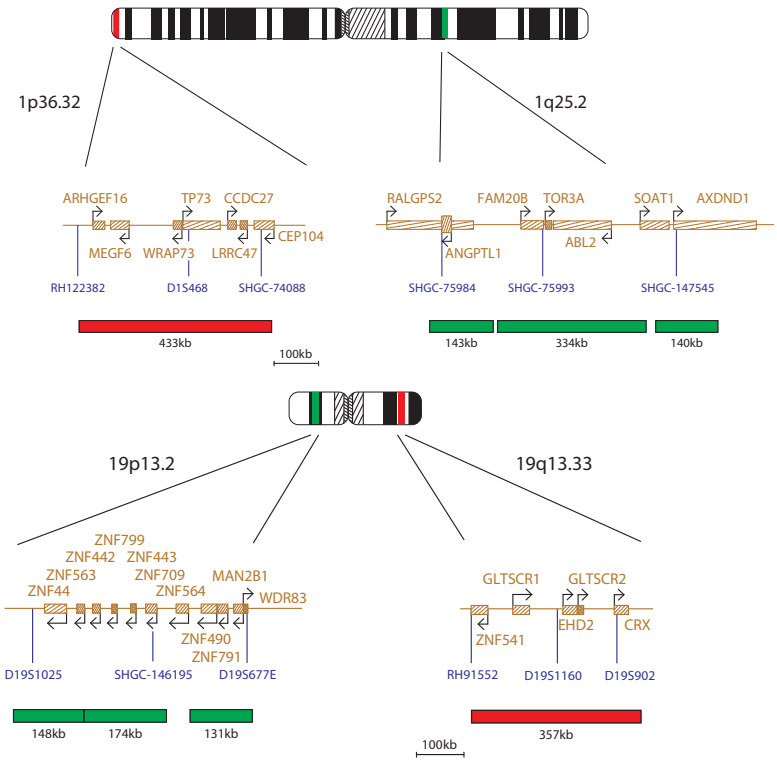
19q13

Deletions of the 1p36.32 region including the TP73 (*tumor protein 73*) gene and deletions of the 19q13.33 region including the GLTSCR1 and GLTSCR2 (*glioma tumor suppressor candidate region genes 1 and 2*) genes are frequently reported in cases of glial tumours.

Astrocytomas and oligodendrogliomas are the most common gliomas that arise from glial cells. They make up about 40% of all CNS tumours[1] and more than 60% of primary brain cancers[2].

Concurrent losses, 'co-deletion', of the 1p36.32 and 19q13.33 regions are reported in approximately 80% of oligodendrogliomas, two-thirds of anaplastic oligodendrogliomas, as well as subsets of oligoastrocytomas and anaplastic oligoastrocytomas[3,4]; the majority of these losses have been shown to be mediated by the presence of an unbalanced t(1;19)(q10;p10) translocation. The presence of a 1p and 19q co-deletion is a strong prognostic factor in these diseases, where it is associated with improved prognosis and responsiveness to therapy[5].

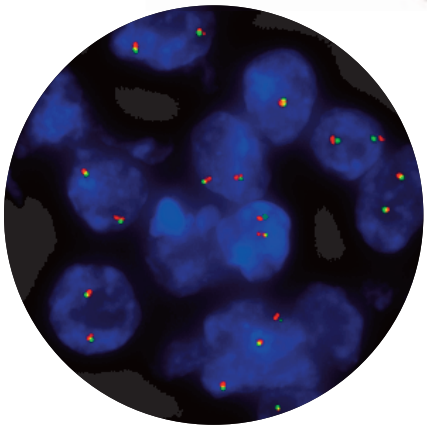
1p and 19q co-deletion has also been shown to occur in a subset of extraventricular neurocytomas, and may be associated with aggressive histology in these tumours[6].



REFERENCES

1. GLOBOCAN CBTRUS (2004). Central Brain Tumor Registry of the United States
2. Thompson L.. Ear Nose Throat J. 2006 Feb;85(2):74
3. Vogazianou AP *et al.*,Neuro Oncol. 2010 Jul;12(7):664-78
4. Bromberg JEC. *et al.*, Oncol. 2009. 14:155-163
5. Jenkins RB *et al.*, Cancer Res 2006;66(20):9852-61
6. Rodriguez FJ *et al.*, Brain Pathol 2009;19(4):623-9

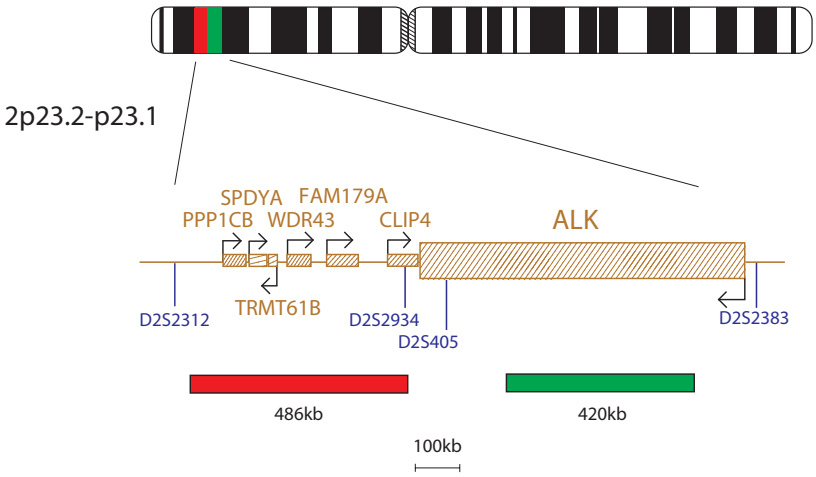
ALK Breakapart



Transforming rearrangements of the ALK (*anaplastic lymphoma receptor tyrosine kinase*) gene at 2p23 have been recognised in a subset of human haematological and solid tissue malignancies[1].

ALK fuses with NPM1 (*nucleophosmin*) in anaplastic lymphoma, resulting in constitutive kinase activity, which inhibits apoptosis and promotes cellular proliferation[2]. In non-small cell lung cancer (NSCLC), approximately 5% of patients will harbour ALK rearrangements, the majority as a result of an inversion involving chromosome 2, inv(2)(p21p23), causing ALK to fuse with the EML4 (*echinoderm microtubule-associated protein like 4*) gene[2,3]. ALK-driven tumours can be treated with crizotinib, a selective small-molecule inhibitor of ALK and its oncogenic variants[3].

ALK translocations have also been reported in a number of other malignancies including inflammatory myofibroblastic tumour[4] and renal medullary carcinoma[5]. Additionally, ALK amplification has been reported as a frequent occurrence in oesophageal cancer[6].



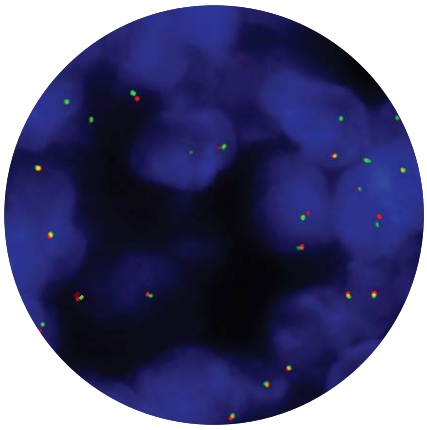
REFERENCES

1. Marileila Varella-Garcia *et al*., Association of molecular pathology: Solid Tumour Review. 2010
2. Takeuchi K *et al*., Clin Cancer Res. 2008;14(20):6618-6624
3. Kwak *et al*., N Engl J Med. 2010;363(18):1693-1703
4. Griffin *et al*,. Cancer Res 1999;59:2776-2780
5. Debelenko *et al*., Mod Pathol. 2011;24(3):430-42
6. Schoppmann SF1 *et al*., Eur J Cancer. 2013;49(8):1876-81

Cytocell an OGT company aquarius

Cat. No. **LPS 015-S** (5 tests)
Cat. No. **LPS 015** (10 tests)

CHOP (DDIT3) Breakapart



Translocations involving the DDIT3 (*DNA-damage-inducible transcript 3*) gene at 12q13 are seen frequently in cases of myxoid liposarcoma.

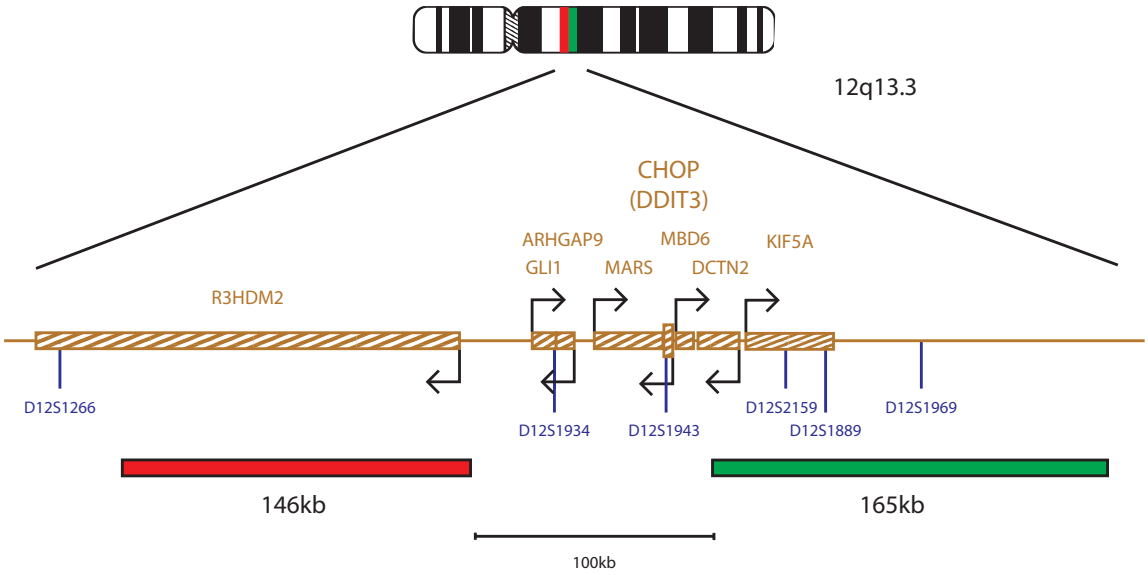
Myxoid liposarcoma (MLS) is the most common subtype of liposarcoma[1] and is characterised by the presence of the FUS-DDIT3 t(12;16)(q13.3;p11) fusion gene. This was first described in 1986[2] and is now well-recognised and is present in at least 95% of cases of MLS[3].

The transcription factor gene DDIT3 is a negative regulator of adipocyte differentiation[4]. The FUS (*FUS RNA binding protein*) gene is a nuclear RNA-binding protein with extensive sequence similarity to EWSR1. The FUS-DDIT3 protein interferes with adipocyte differentiation and favours proliferation over terminal differentiation.

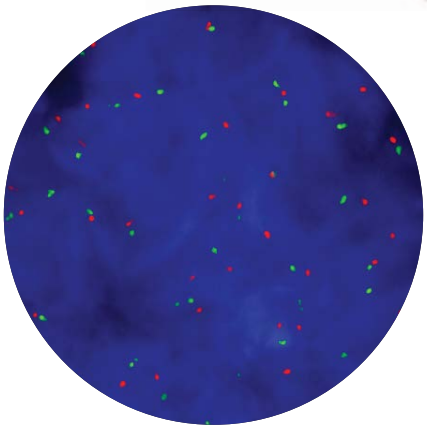
Less commonly, a variant EWSR1-DDIT3 t(12;22)(q13;q12) translocation is seen[6].

REFERENCES

1. Enzinger and Weiss, Soft Tissue Tumors 3rd Ed. St Louis; MO:Mosby, 1995
2. Turc-Carel *et al*., Can Genet Cytogenet 1986;23:291-9
3. Mitelman, Catalog of chromosome aberrations in cancer. 5th Ed. 1995 New York: WileyLiss, Inc. 1994
4. Hunag *et al*., Biol Open. 2012 Aug 15;1(8):705-10
5. Rabbitts *et al*., Nat Genet 1993;4:175-80
6. Antonescu *et al*., Clin Canc Res 2001;7:3977-87



C-MET (MET) Amplification



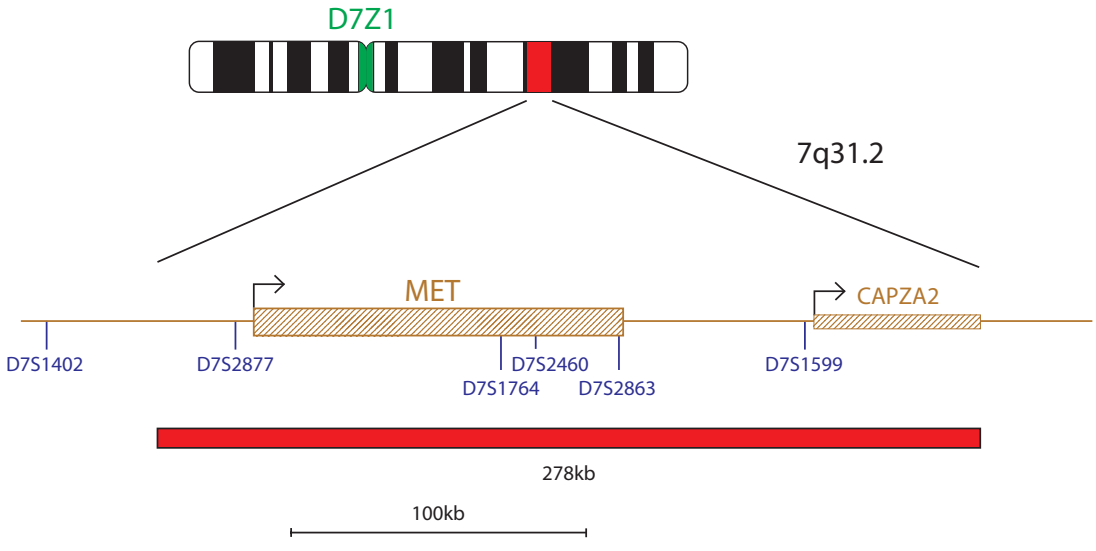
The MET (*MET proto-oncogene, receptor tyrosine kinase*) gene at 7q31.2 encodes a transmembrane tyrosine kinase[1].

The MET gene regulates both cell motility and cell growth[2]; therefore, normal MET protein expression allows stem cells and progenitor cells to grow invasively. This invasive growth is required, in embryos to generate new tissues and in adults to repair wounds or regenerate tissue, such as the liver[3].

The MET gene has been shown to be overexpressed in many tumours including ovarian[4], breast[5], lung[6], thyroid[7], stomach[8], pancreatic,[9,10] and colon[11,12]. This overexpression correlates with a poor prognosis[4,13,14]. In breast cancers, MET was only shown to be co-expressed with ERBB2 in 50% of patients, indicating that it has a significant impact on tumour aggressiveness independently of ERBB2[14]. In recurrent/metastatic gastric cancer, MET gene amplification has been shown to be significantly associated with an unfavourable clinical outcome[15].

REFERENCES

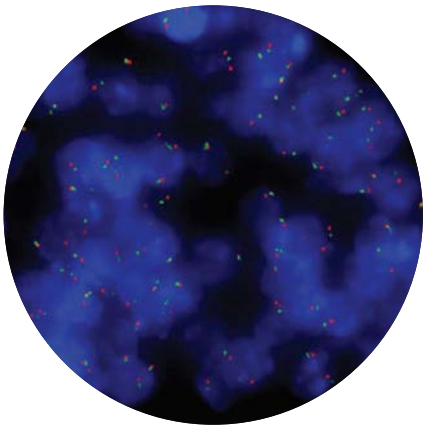
1. Dean M *et al*., Nature 1985;318:385-8
2. Gherardi E, Stoker M, Cancer Cells 1991;3(6):227-32
3. Boccaccio C, Comoglio PM, Nat Rev Cancer 2006;6(8):637-45
4. Sawada K *et al*., Cancer Res 2007;67(4):1670-9
5. Carracedo A *et al*., Breast Cancer Res 2009;11(2):402
6. Zucali PA *et al*., Ann Oncol 2008;19(9):1605-12
7. Di Renzo MF *et al*., Oncogene 1992;7:2549-53
8. Kuniyasu H *et al*., Int J Cancer 1993;55(1):72-5
9. Ebert M *et al*., Cancer Res 1994;54:5775-8
10. Di Renzo MF *et al*., Cancer Res 1995;55:1129-38
11. Liu C *et al*., Oncogene 1992;7(1):181-5
12. Di Renzo MF *et al*., Clin Cancer Res 1995;1:147-54
13. Miyamoto *et al*., Br J Cancer. 2011 Jun 28;105(1):131-8
14. Lengyel E *et al*., Int J Canc 2005;113:678-82
15. An X *et al*., Cancer. 2014;120(5):675-82



Cytocell an OGT company aquarius

Cat. No. **LPS 003-S** (5 tests)
Cat. No. **LPS 003** (10 tests)

EGFR Amplification



The EGFR (*epidermal growth factor receptor*) gene at 7p11.2, encodes a type 1 tyrosine kinase receptor for members of the epidermal growth factor family. Binding of the epidermal growth factor receptor and epidermal growth factor proteins lead to signal transduction cascades and regulate signaling pathways to control cellular proliferation[1].

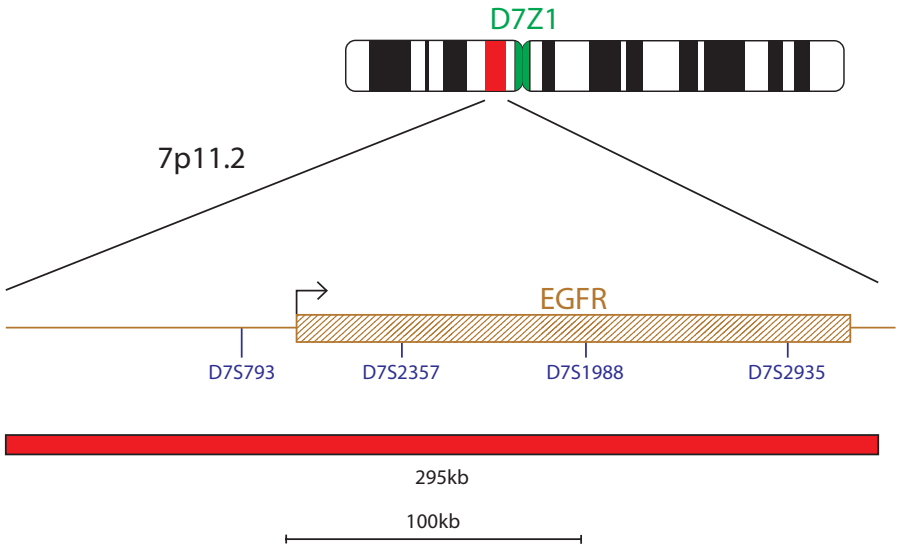
Abnormally-elevated EGFR kinase activity can lead to proliferative diseases such as non-small-cell lung carcinoma (NSCLC), which accounts for 80-85% of all lung cancers[2], and less frequently breast cancer[3], amongst others.

There are a number of EGFR-inhibitor drugs in clinical use, for example: gefitinib and erlotinib in NSCLC, lapatinib in breast cancer or cetuximab in colorectal cancer[4,5]. Approximately 10% of lung cancer patients show a rapid and dramatic response to these tyrosine kinase inhibitors (TKIs)[6,7].

FISH has been shown to be useful for determining the amplification status of EGFR in NSCLC, aiding the selection of patients for treatment with EGFR TKIs[8].

REFERENCES

1. Voldborg *et al*., Annals of Oncology 1997;8: 1197-1206
2. Jemal A *et al*., CA Cancer J Clin 2006;56:106-30
3. Bhargava R *et al*., Modern Path 2005;18:1027-33
4. Hegymegi-Barakonyi B, Curr Opin Mol Ther 2009;11(3):308-21
5. Jonker D *et al*., N Engl J Med 2007; 357:2040-2048
6. Lynch TJ *et al*., N E J Med 2004;350:2129-39
7. Pao W *et al*., Proc Natl Acad Sci USA 2004;101(36):13306-11
8. Hirsch FR *et al*., JCO 2008;26(20): 3351-7

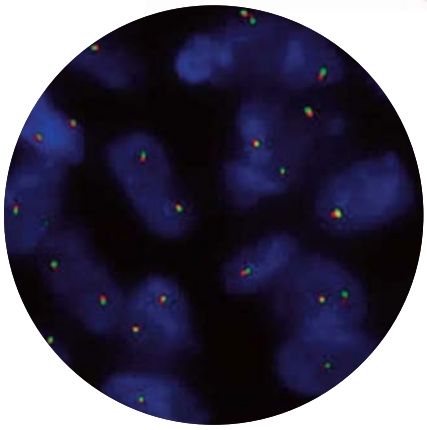


Cytocell an OGT company aquarius

Cat. No. **LPS 020-S** (5 tests)

Cat. No. **LPS 020** (10 tests)

EML4 Breakapart

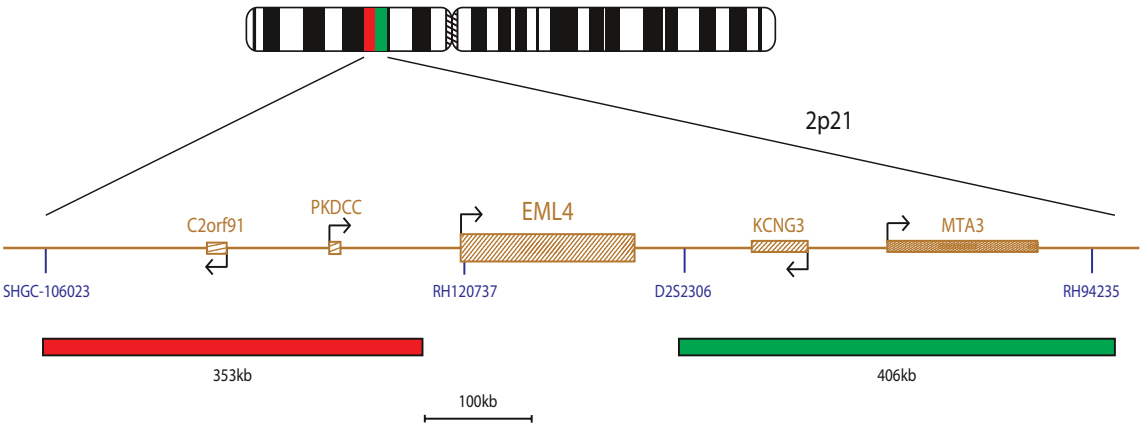


The protein encoded by the EML4 (*echinoderm microtubule associated protein like 4*) gene at 2p21 is involved in microtubule formation and stabilisation[1].

A novel gene fusion of EML4 and ALK (*anaplastic lymphoma receptor tyrosine kinase*) has been identified in patients with non-small cell lung cancer (NSCLC). The EML4-ALK fusion results from an inversion within chromosome 2p, inv(2)(p21p23), and is detected in approximately 5% of NSCLC cases[2,3,4]. ALK-driven tumours can be treated with crizotinib, a selective small-molecule inhibitor of ALK and its oncogenic variants[5].

REFERENCES

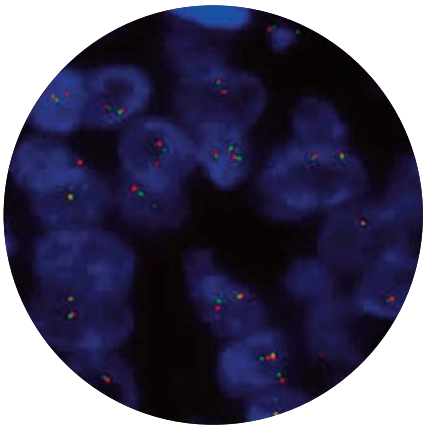
1. Xuchao Zhang *et al*., Mol Cancer Res 2010;9:188
2. Lin *et al*., Mol Cancer Res 2009;7(9):1466-1476
3. Martelli *et al*., AJP 2009;174(2):661-670
4. Takaaki S *et al*., Eur J Cancer. 2010; 46(10): 1773-1780
5. Kwak *et al*.,N Engl J Med. 2010;363(18):1693-1703



Cytocell an OGT company aquarius

Cat. No. **LPS 006-S** (5 tests)
Cat. No. **LPS 006** (10 tests)

EWSR1 Breakapart



Rearrangements involving the EWSR1 (*EWS RNA binding protein 1*) gene at 22q12.2 are seen in a wide variety of mesenchymal lesions, and involve a large number of recognised partner genes.

Ewing sarcoma is the second most frequent primary bone cancer in patients under 20 years of age[1]. Approximately 85% of Ewing sarcomas are characterized by a t(11;22)(q24;q12.2) translocation involving EWSR1 and FLI1[2]. Approximately 10% of the remaining cases have a variant t(21;22)(q22.3;q12.2) translocation involving EWSR1 and ERG[3]. The remaining cases involve one of the many other EWSR1 translocation partners such as 7p22 (ETV1), 17q12 (ETV4) or 2q36 (FEV) translocations with EWSR1[4].

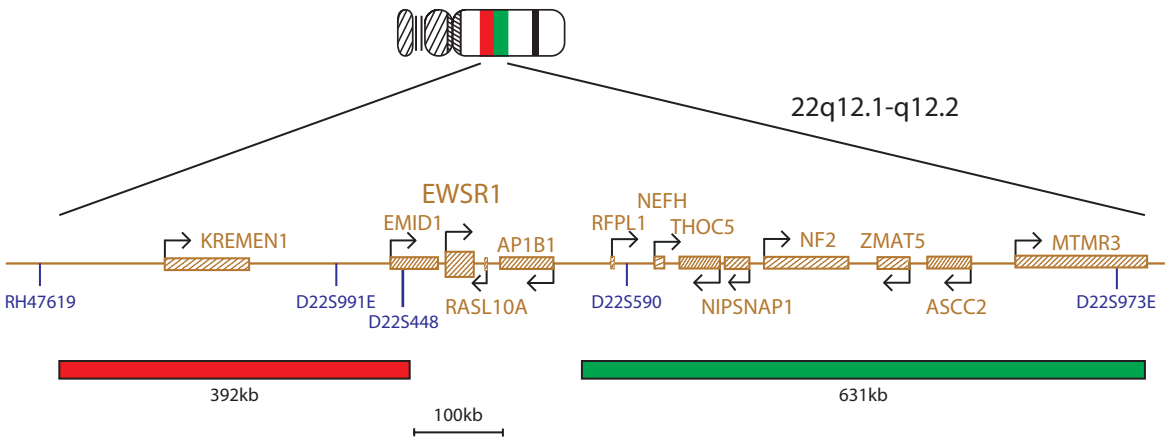
Recurrent EWSR1 rearrangements are also recognised in a number of other conditions, including: translocations with WT1 via the t(11;22)(p13;q12.2) in desmoplastic small round cell tumours[5,6]; translocations with DDIT3 via the variant t(12;22)(q13;q12.2) in myxoid liposarcoma[7] and t(9;22)(q22;12.2) translocations in extraskeletal myxoid chondrosarcoma, which fuse the EWSR1 gene with the NR4A3 gene[8].

The EWSR1 breakapart probe can also be used to distinguish clear cell sarcoma from melanoma, a distinction that is difficult to make via either histology or immunohistology. The EWS-ATF1 translocation, t(12;22)(q13;q12), has been identified in more than 90% of clear cell sarcoma, yet has not been observed in melanoma[9,10].

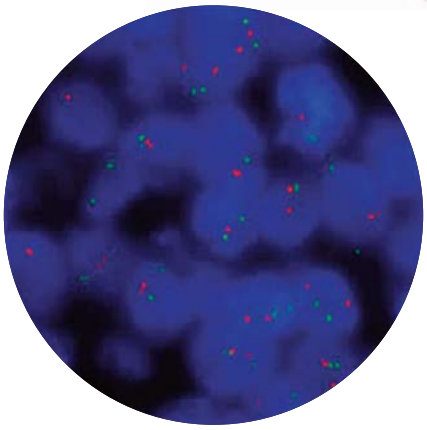
This breakapart probe has been designed to allow detection of EWSR1 rearrangements regardless of the partner gene.

REFERENCES

1. Bernstein M *et al*., Oncologist 2006;11(5):503-19
2. Turc-Carel C *et al*., Cancer Genet Cytogenet 1988;32:229-38
3. Sorensen PH *et al*., Nat Genet. 1994;6(2):146-51
4. Martine P *et al*., Oncogene 1997;14:1159-1164
5. Borden EC *et al*., Clin Canc Res 2003;9:1941-56
6. Sandberg AA, Bridge JA, Cancer Genet Cytogenet 2000;123(1):1-26
7. Fritchie KJ *et al*., Am J Clin Pathol 2012;137:229-239
8. Sciot R *et al*., Mod Pathol. 1995;8:765-768
9. Patel RM *et al*., Modern Path 2005;18:1585-90
10. Mavrogenis AF *et al*., Hippokratia. 2013; 17(4): 298-302



EWSR1/ERG Translocation, Dual Fusion

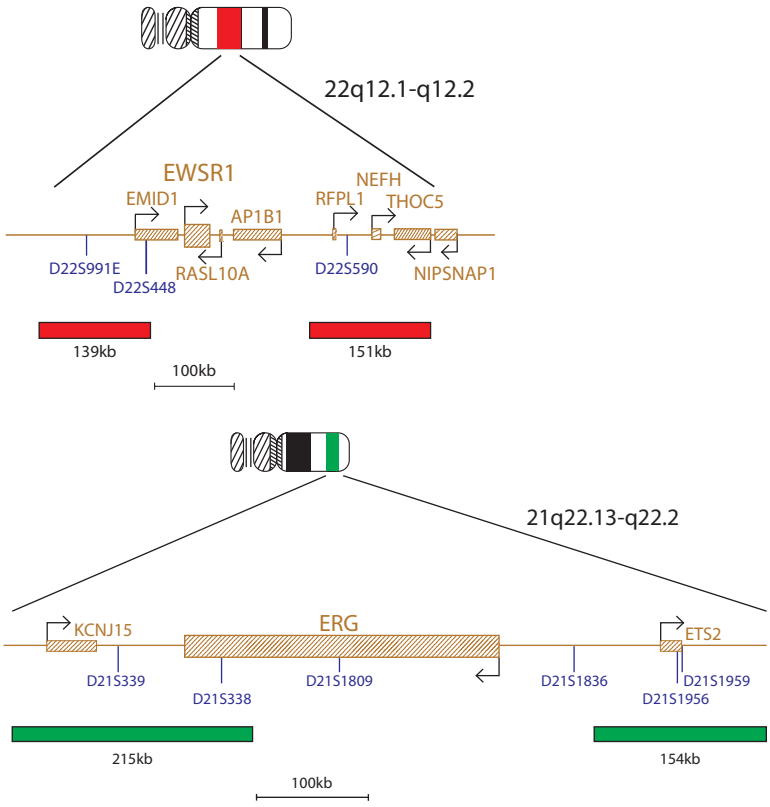


Ewing sarcoma is the second most frequent primary bone cancer in patients under 20 years of age[1].

Approximately 10% of Ewing sarcomas will have a t(21;22)(q22.3;q12.2) translocation involving EWSR1 and ERG (*v-ets avian erythroblastosis virus E26 oncogene homologue*)[2]. The majority of cases, up to 85%, of Ewing sarcoma will show a t(11;22)(q24;q12.2) translocation involving the EWSR1 and FLI1 genes[3]. The remaining cases involve one of the many other EWSR1 translocation partners such as 7p22 (ETV1), 17q12 (ETV4) or 2q36 (FEV) translocations with EWSR1[4].

REFERENCES

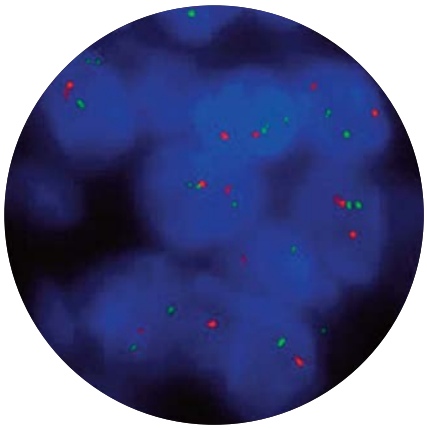
1. Bernstein M *et al*., Oncologist 2006;11(5):503-19
2. Sorensen PH *et al*., Nat Genet. 1994;6(2):146-51
3. Turc-Carel C *et al*., Cancer Genet Cytogenet 1988;32:229-38
4. Martine P *et al*., Oncogene 1997;14:1159-1164



Cytocell an OGT company aquarius

Cat. No. **LPS 007-S** (5 tests)
Cat. No. **LPS 007** (10 tests)

FLI1/EWSR1 Translocation, Dual Fusion

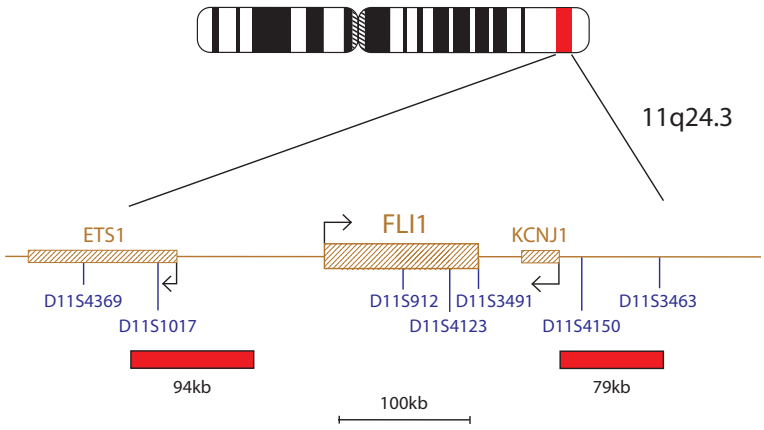


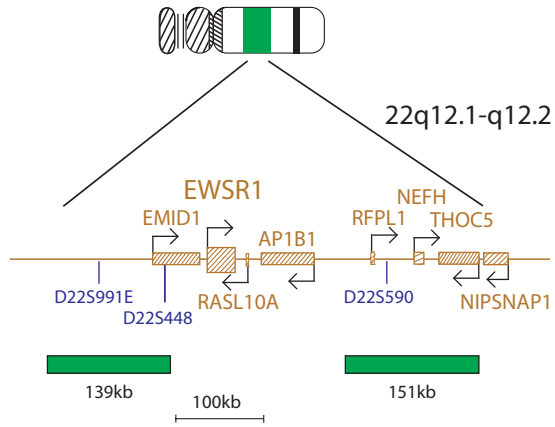
Ewing sarcoma is the second most frequent primary bone cancer in patients under 20 years of age[1].

Approximately 85% of Ewing sarcomas are characterised by a t(11;22)(q24;q12.2) translocation involving the EWSR1 and FLI1 (*Fli-1 proto-oncogene, ETS transcription factor*) genes[2]. Approximately 10% of the remaining cases have a variant t(21;22)(q22.3;q12.2) translocation involving EWSR1 and ERG[3]. The remaining cases involve one of the many other EWSR1 translocation partners such as 7p22 (ETV1), 17q12 (ETV4) or 2q36 (FEV) translocations with EWSR1[4].

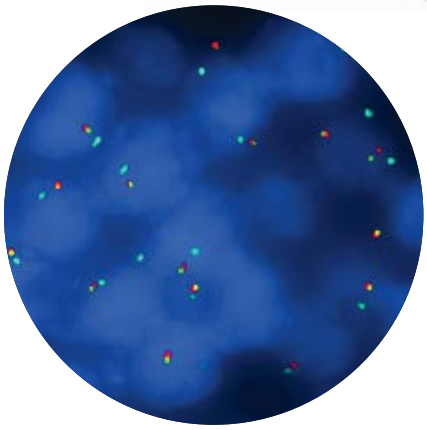
REFERENCES

1. Bernstein M *et al*., Oncologist 2006;11(5):503-19
2. Turc-Carel C *et al*., Cancer Genet Cytogenet 1988;32:229-38
3. Sorensen PH *et al*., Nat Genet. 1994;6(2):146-51
4. Martine P *et al*., Oncogene 1997;14:1159-1164





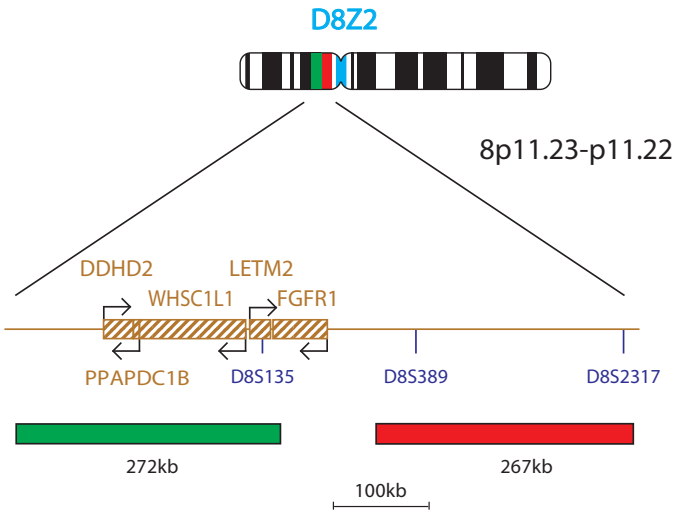
FGFR1 Breakapart/Amplification



The FGFR1 (*fibroblast growth factor receptor 1*) gene, at 8p11, has been shown to be amplified in approximately 10% of breast cancers[1,2], in approximately 20% of squamous cell carcinomas of the lung (SCCL)[3] and in approximately 9% of non-small-cell lung cancers (NSCLC)[4]. The FGFR1 gene is also involved in translocations in patients with 8p11 myeloproliferative syndrome[5].

Amplification of FGFR1 has been shown to be associated with a poor outcome in breast cancer, as over-expression of the gene product has been implicated in early relapse[6]. Amplification of FGFR1 has also been associated with a poor prognosis in both squamous cell carcinoma of the lung (SCCL) and non-small-cell lung cancer (NSCLC)[7,8].

FGFR1 is a receptor tyrosine kinase for fibroblast growth factors[9]. FGFR1 rearrangements are associated with 8p11 myeloproliferative syndrome (EMS)/stem cell leukaemia-lymphoma syndrome. A number of gene fusions that have constitutive tyrosine kinase activity have been described in EMS, including: FGFR1-ZNF198, the most common, via a t(8;13)(p11;q12) translocation; FGFR1-CEP10 via a t(8;9)(p11;q33) translocation, FGFR1-FOP via a t(6;8)(q27;p11) translocation and FGFR1-BCR via a t(8;22)(p11q22) translocation[10,11].



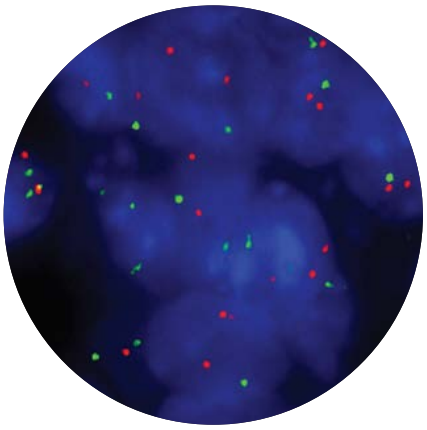
REFERENCES

1. Letessier A *et al*., BMC Cancer 2006, 6:245
2. Theillet *et al*., Genes Chromosomes Cancer 1993;7:219-26
3. Wiess *et al*., Sci Transl Med. 2010 2(62): 62ra93
4. Macdonald D *et al*, Acta Haematol 2002;107:101-107
5. Macdonald *et al*., Leukemia 1995;9:1628-30
6. Turner N *et al*., Cancer Res 2010;70(5):2085-94
7. Kim HR *et al*., J Clin Oncol. 2013;31(6):731-7
8. Seo AN, *et al*., Virchows Arch. 2014;465(5):547-58
9. Groth & Lardelli, Int. J. Dev. Biol. 2002 46: 393-400
10. Xiao *et al*., Nature Genet 1998;18:84-7
11. Keersmaecker & Cools. Leukemia 2006;20(2):200-205

Cytocell an OGT company aquarius

Cat. No. **LPS 001-S** (5 tests)
Cat. No. **LPS 001** (10 tests)

HER2 (ERBB2) Amplification



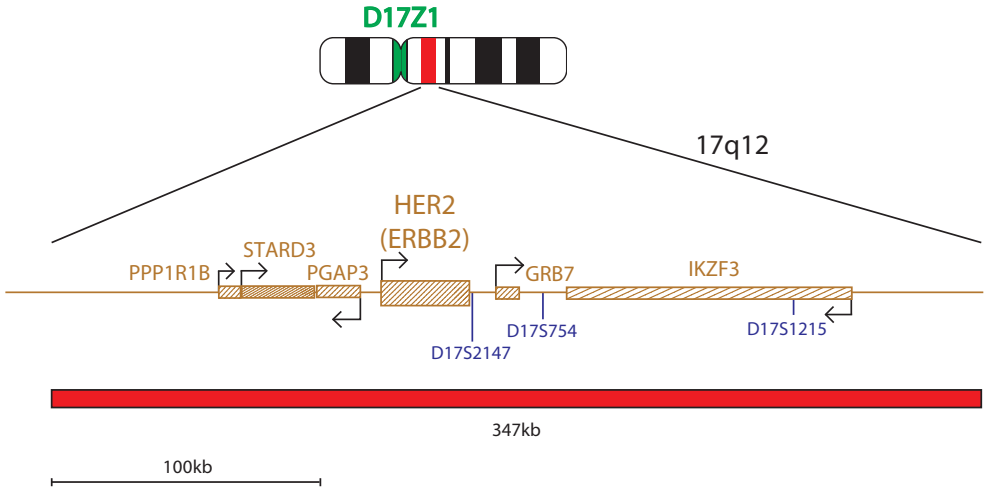
The ERBB2 (*erb-b2 receptor tyrosine kinase 2*) gene, located at 17q12, is a member of the epidermal growth factor (EGF) receptor family[1].

ERBB2 amplification is seen in approximately 15% of breast cancers[2] and, in the absence of therapy, is associated with a poor prognosis for the patient[3]. Treatment of patients with ERBB2 amplification using the monoclonal antibody trastuzumab has been shown to be effective in the treatment of breast cancer, increasing overall survival time by suppressing ERBB2 activity and leading to cell death[4,5].

Similar results have been obtained for a variety of other malignant neoplasms overexpressing ERBB2, including some ovarian[6], stomach[7,8], salivary gland[9] and lung cancers[10].

REFERENCES

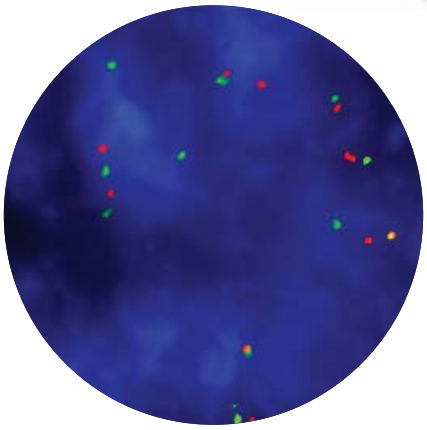
1. Coussens L, Yang-Feng TL *et al*., Science 1985;230(4730):1132-9
2. Slamon DJ *et al*., Science 1987;235(4785):177-82
3. López-Guerrero JA *et al*., Int J Cancer. 2006;118(7):1743-9
4. Kauraniemi P *et al*., Oncogene 2004;23(4):1010-3
5. Thuy Vu *et al*., Front Oncol. 2012;2:62
6. Slamon DJ *et al*., Science 1989;244(4905):707-12
7. Gravalos C, Jimeno A, Ann Oncol 2008;19(9):1523-9
8. Boku N. Gastric Cancer. 2014;17(1):1-12
9. Vidal L *et al*., Head Neck 2009;31(8):1006-12
10. Ugocsai *et al*., Anticancer Res. 2005;25(4):3061-6



Cytocell an OGT company aquarius

Cat. No. **LPS 016-S** (5 tests)
Cat. No. **LPS 016** (10 tests)

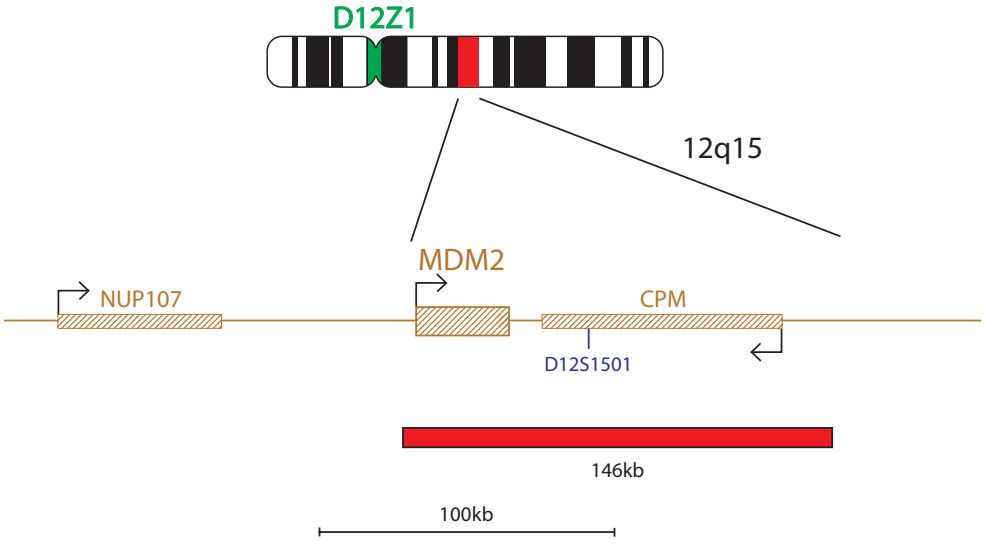
MDM2 Amplification



The MDM2 (*MDM2 proto-oncogene, E3 ubiquitin protein ligase*) gene at 12q15, when overexpressed, enhances the tumourigenic potential of cells. MDM2 overexpression is seen in many cancer types with an overall frequency of gene amplification of around 7%[1,2].

MDM2 protein overexpression often results from MDM2 gene amplification, which has been reported in well-differentiated liposarcoma, osteosarcoma, colorectal cancer, non-small cell lung cancer and glioma, amongst many others, with the prognostic implications of the presence of MDM2 amplification varying with the tumour type[2,3,4,5,6].

The MDM2 oncogene product forms a tight complex with the p53 tumour suppressor protein that inhibits p53-mediated transactivation, leading to escape from p53 regulated growth control[7]. A number of small-molecule inhibitors that block the MDM2-p53 interaction, thereby reactivating p53 function, have advanced into human cancer clinical trials[8,9].



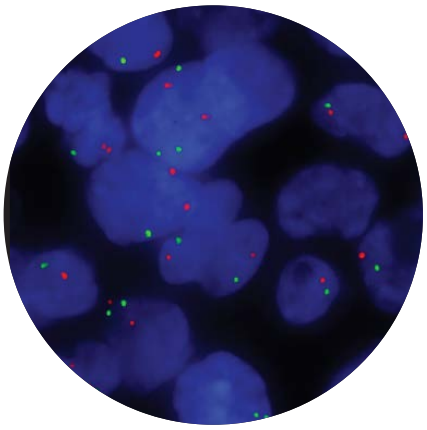
REFERENCES

1. Forslund *et al*., Mol Cancer Res. 2008 Feb;6(2):205-11
2. Momand J, Nuc Acid Res 1998;26(15):3453-9
3. Weaver J *et al*., Modern Path 2008;21(8):943-9
4. Sirvent N *et al*., Am J Surg Pathol 2007;31(10):1476-98
5. Onel K *et al*., Mol Cancer Res. 2004;2:1-8
6. Rayburn E *et al*., Curr Cancer Drug Targets. 2005;5:27-41
7. Momanad J *et al*., Cell 1992;69(7):1237-45
8. Vassilev LT, Trends Mol Med 2007;13(1):23-31
9. Zhao Y *et al*., J Med Chem. 2015;58:1038-52

Cytocell an OGT company aquarius

Cat. No. **LPS 009-S** (5 tests)
Cat. No. **LPS 009** (10 tests)

N-MYC (MYCN) Amplification



The proto-oncogene MYCN (*v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog*) located at 2p24.3, is a transcription factor that plays a role in regulation of cell growth and proliferation.

MYCN mainly expressed in the developing nervous system and is critical during neural crest embryogenesis; it then becomes rapidly down-regulated as tissues become terminally differentiated and growth-arrested[1]. Over-expression of MYCN appears to block differentiation and increase cell proliferation[2].

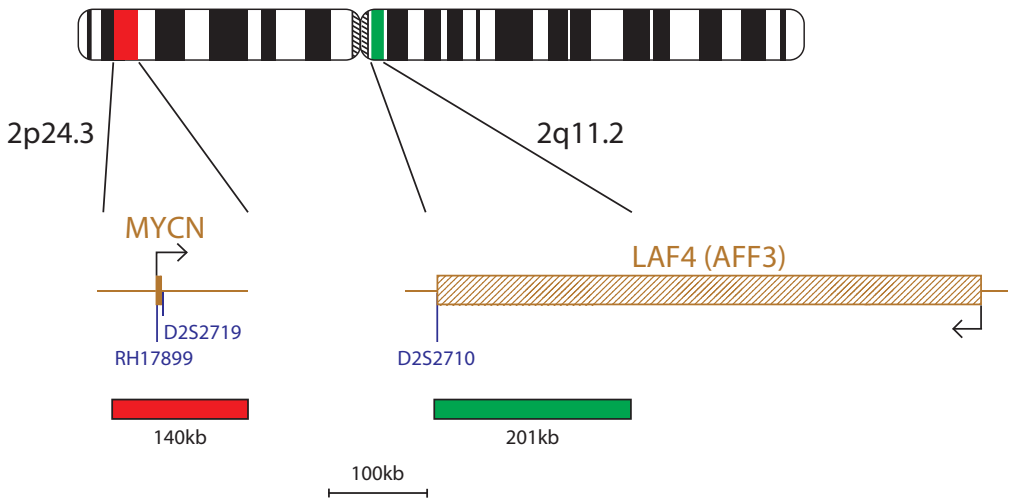
In neuroblastoma, the most common extracranial solid tumour in childhood, MYCN gene amplification is seen in 16% to 25% of tumours and is associated with a poor clinical outcome[3,4].

In medulloblastoma, the most common malignant brain tumour in childhood, MYCN gene amplification is seen mainly within SHH and Group 4 medulloblastomas and is associated with a less favourable outcome[5,6]

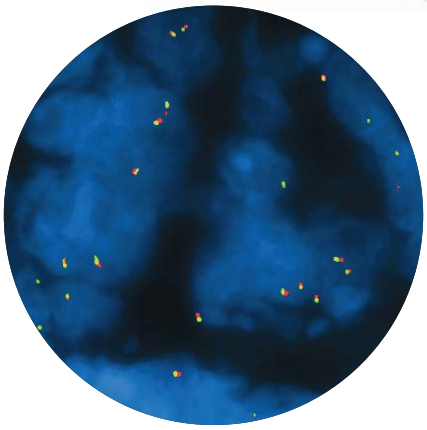
Amplification of the MYCN gene has also been reported in other cancers including a subset of unilateral retinoblastoma tumours in the absence of detectable RB1 mutations[7].

REFERENCES

1. Thomas WD *et al.*, Int J of Bioch and Cell Biol 2004;36(5):771-5
2. Look *et al.*, J Clin Oncol. 1991 Apr;9(4):581-91
3. Ambros PF *et al.*, Br J Cancer. 2009;100:1471-82
4. Cheung NK *et al.*, Nat Rev Cancer. 2013;13:397-411
5. Shih *et al.*, J Clin Oncol 2014;32:886-896
6. Kool M *et al.*, Acta Neuropathol. 2012;123:473-84
7. Rushlow D *et al.* The Lancet Oncology. 2013;14(4):327-334



PAX3 Breakapart and PAX7 Breakapart



PAX7 Breakapart

Translocations involving the FOXO1 (*forkhead box O1*) gene at 13q14 and either the PAX3 (*paired box 3*) gene at 2q36.1 or the PAX7 (*paired box 7*) gene at 1p36.13 are seen frequently in cases of alveolar rhabdomyosarcoma

Rhabdomyosarcoma is the most common soft-tissue sarcoma seen in children and younger adults with two major histological subtypes: alveolar rhabdomyosarcoma (ARMS) and embryonal rhabdomyosarcoma (ERMS). FOXO1 rearrangements are recognised recurrent abnormalities seen in ARMS, but not seen in ERMS,[1,2].

Approximately 55% of cases of ARMS are associated with a PAX3-FOXO1 rearrangement via a t(2;13)(q36.1;q14) translocation and 22% of cases of ARMS are associated with a PAX7-FOXO1 rearrangement via a t(1;13)(p36;q14) translocation[3]. These translocations lead to the fusion of transcription factor FOXO1 to the transcription factors PAX3 and PAX7 located at 2q36.1 and 1p36.13 respectively[2].

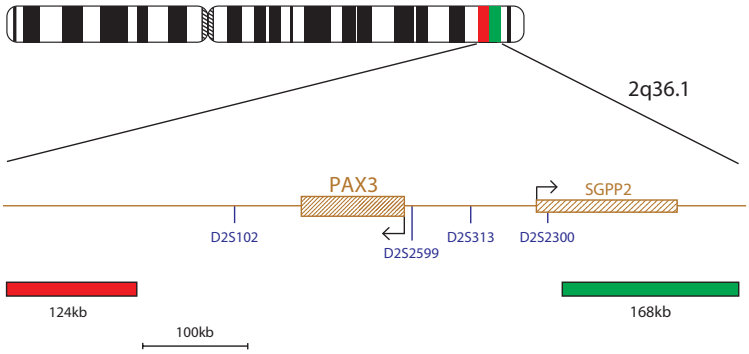
Studies have shown that ARMS patients with PAX-FOXO1 rearrangements have an inferior outcome compared to ERMS patients, whereas ARMS patients without PAX-FOXO1 rearrangements show similar outcomes to ERMS[2,4].

A subset of patients with ARMS may show fusion gene amplification. This is most commonly associated with the presence of PAX7-FOXO1 rearrangements and has been shown to be associated with significantly improved outcome over ARMS patients with PAX-FOXO1 re-arrangements without fusion gene amplification[5].

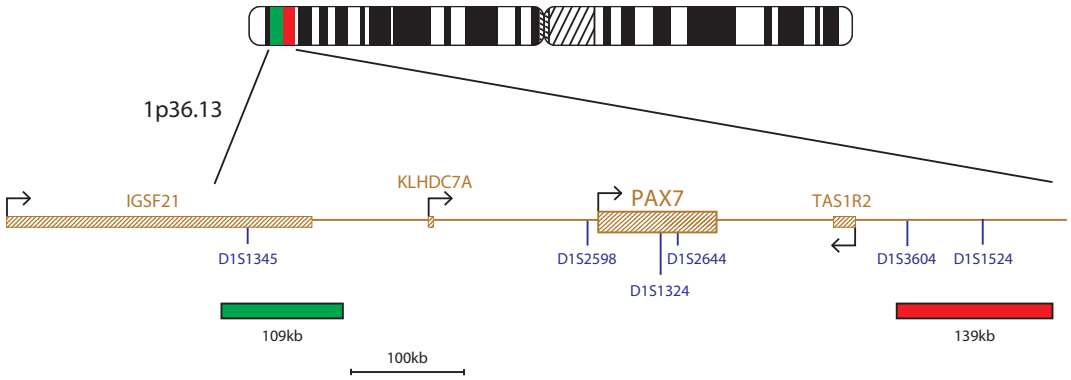
REFERENCES

1. Anderson *et al*., Am J Pathol. 2001 Sep;159(3):1089-96
2. Jothi *et al*., Mol Cancer Ther. 2013 Dec;12(12):2663-74
3. Sorensen PH *et al*.,J Clin Oncol. 2002;20(11):2672-9
4. Skapek *et al*., Pediatr Blood Cancer. 2013 Sep;60(9):1411-7
5. Duan *et al*., Genes Chromosomes Cancer. 2012 Jul; 51(7):662-674

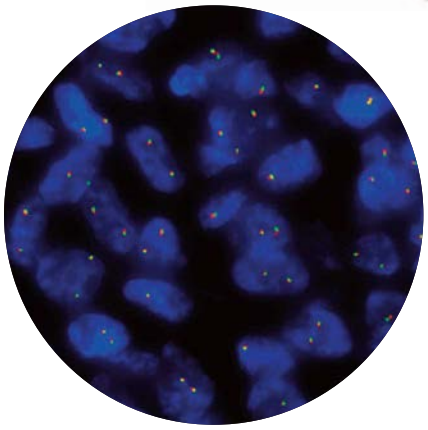
PAX3 Cat. No. **LPS 012**



PAX7 Cat. No. **LPS 013**



ROS1 Breakapart



The ROS1 (*ROS proto-oncogene 1, receptor tyrosine kinase*) gene at 6q22 is an ALK (*anaplastic lymphoma receptor tyrosine kinase*) gene paralogue which encodes a type I integral membrane protein with tyrosine kinase activity[1].

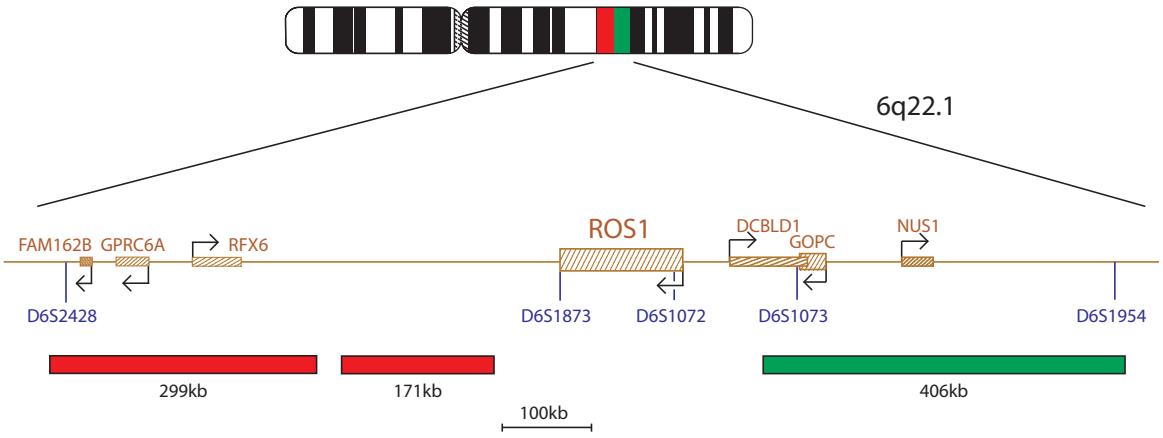
ROS1 rearrangements define a molecular subset of non-small cell lung cancer (NSCLC) and are seen in approximately 2% of patients with NSCLC[2]. A number of partner genes have been identified, including SLC34A2, CD74 and SDC4[3]. It has been shown that these ROS1 fusions activate the pSTAT3, PI3K/AKT/mTOR and SHP-2 phosphatase pathways[4,5].

NSCLC patients with ROS1 rearrangements have been shown to respond to treatment with ALK/MET tyrosine kinase inhibitors, such as crizotinib[6].

ROS1 rearrangements, with the fusion partner GOPC, were originally reported in glioblastoma, but have now also been detected on cholangiocarcinoma, ovarian cancer and NSCLC patient samples[7-9].

REFERENCES

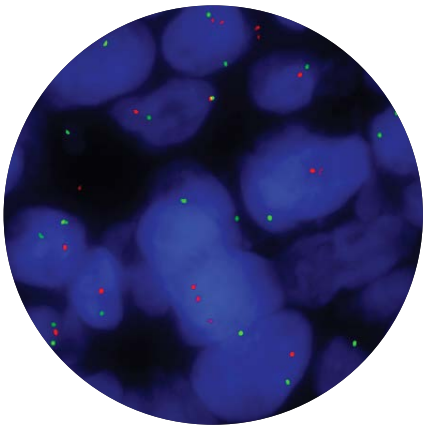
1. Matsushime H *et al*., Mol Cell Biol 1986;6:3000-4
2. Bergethon K *et al*., J Clin Oncol 2012;30(8):863-70
3. Davies KD *et al*., Cancer Res 2012;72(8):1538-7445
4. Birchmeier C *et al*., Proc Natl Acad Sci 1987;84:9270-9274
5. Ou SH *et al*., Expert Rev Anticancer Ther 2012;12(4):447-56
6. Shaw, A.T. *et al*., 2014. 371(21), pp.1963-71
7. Gu TL *et al*., PLoS One 2011;6: e15640
8. Charest A *et al*., Genes Chromosomes Cancer 2003;37:58-71
9. Davies, K.D. & Doebele, R.C., 2013. Clinical cancer 19(15), pp.4040-4045



Cytocell an OGT company aquarius

Cat. No. **LPS 010-S** (5 tests)
Cat. No. **LPS 010** (10 tests)

SRD (CHD5) Deletion



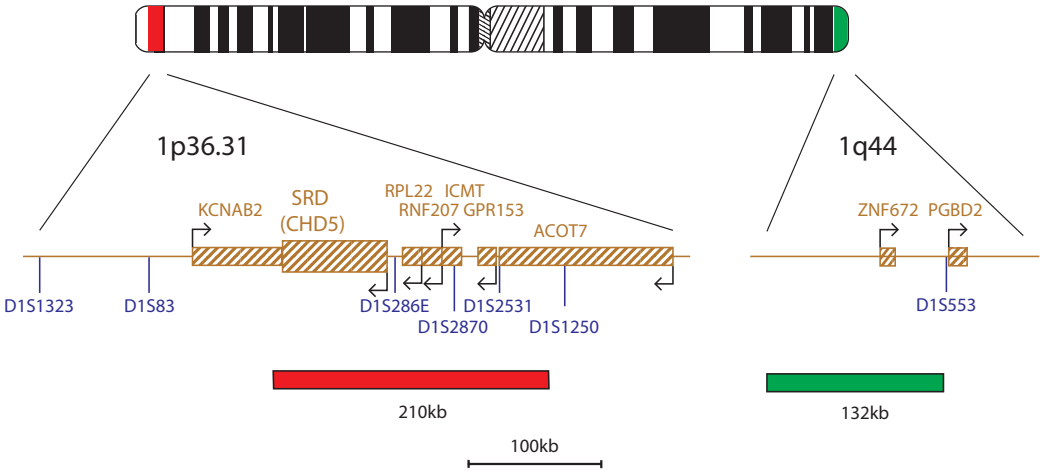
Deletions of the 1p36 region, including the CHD5 (*chromodomain helicase DNA binding protein 5*) gene are seen in a number of human cancers[1].

The CHD5 gene acts as a tumour suppressor, and has been shown to be commonly deleted in neuroblastomas[2]. Deletion of the short arm of chromosome 1 is one of the most characteristic genetic changes in neuroblastoma, the most common tumour of infants, which accounts for around 8-10% of childhood cancers and 15% of childhood cancer deaths[3]. The CHD5 gene has been characterised as the lead tumour suppressor candidate from the 1p36 smallest region of consistent deletion (SRD) region in neuroblastoma[4].

Deletions of this gene have also been reported in gliomas as well as breast, lung, ovarian, gastric, laryngeal, gallbladder, prostate and colorectal cancers[3].

REFERENCES

1. Kolla V, *et al*. Cancer Res. 2014;74(3):652-8.
2. Papaioannou, G., 2005Cancer Imaging, 5(1), pp.116-127
3. Fujita *et al*., J Natl Cancer Inst 2008;100:940-9
4. Bagchi, Mills Canc Res 2008;68(8):2551-6

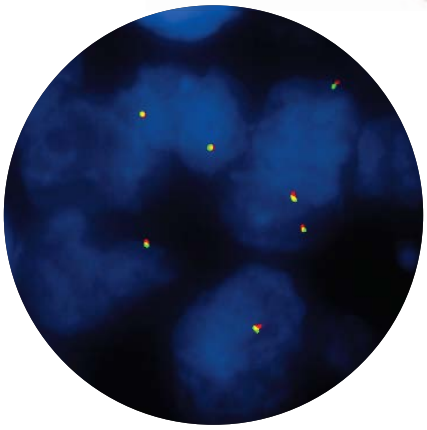


Cytocell an OGT company aquarius

Cat. No. **LPS 014-S** (5 tests)

Cat. No. **LPS 014** (10 tests)

SYT (SS18) Breakapart

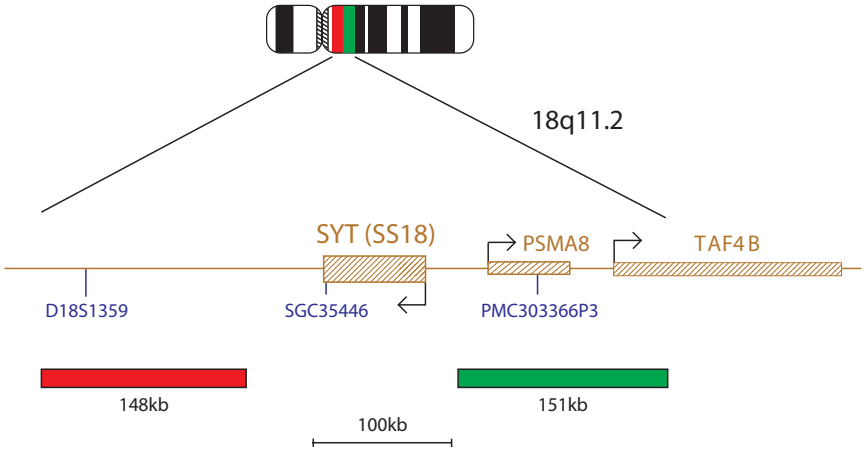


Rearrangements involving the SS18 (*synovial sarcoma translocation, chromosome 18*) gene located at 18q11.2 are seen in more than 90% of synovial sarcomas[1].

Synovial sarcomas account for up to 10% of soft-tissue sarcomas, typically arising in the para-articular regions in adolescents and young adults[2]. The tumour is characterised by the presence of a t(X;18)(p11;q11.2) translocation[3,4].

The translocation fuses the SS18 gene to either one of two highly homologous genes at Xp11: SSX1 (*synovial sarcoma X breakpoint 1*) or SSX2 (*synovial sarcoma X breakpoint 2*). In less than 1% of cases, SS18 will be fused to a third gene, SSX4[5].

SYT-SSX1 and SYT-SSX2 are thought to disrupt transcription and the subsequent expression of specific target genes[6,7].



REFERENCES

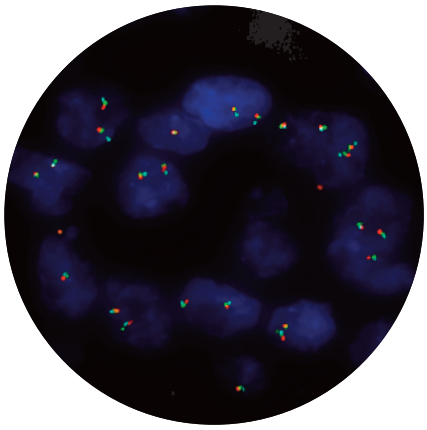
1. Nagao K, *et al*., Am J Pathol. 1996;148(2):601-9
2. Bhattacharya, *et al*., Int J App Med Res. 2016; 6(1):63-65
3. Turc-Carel C, *et al*. Proc Natl Acad Sci 1987;84(7):1981-5
4. Sreekantaiah *et al*., Am J Pathol 1994;144:1121-34
5. Ladanyi *et al*., Canc Res 2002;62:135-40
6. Ladanyi *et al*., Diagn Mol Pathol 1995;4:162-73
7. Sorensen & Triche, Semin Cancer Biol 1996;7:3-14

Cytocell an OGT company aquarius

Cat. No. **LPS 021-S** (5 tests)

Cat. No. **LPS 021** (10 tests)

TMPRSS2/ERG Deletion/Breakapart

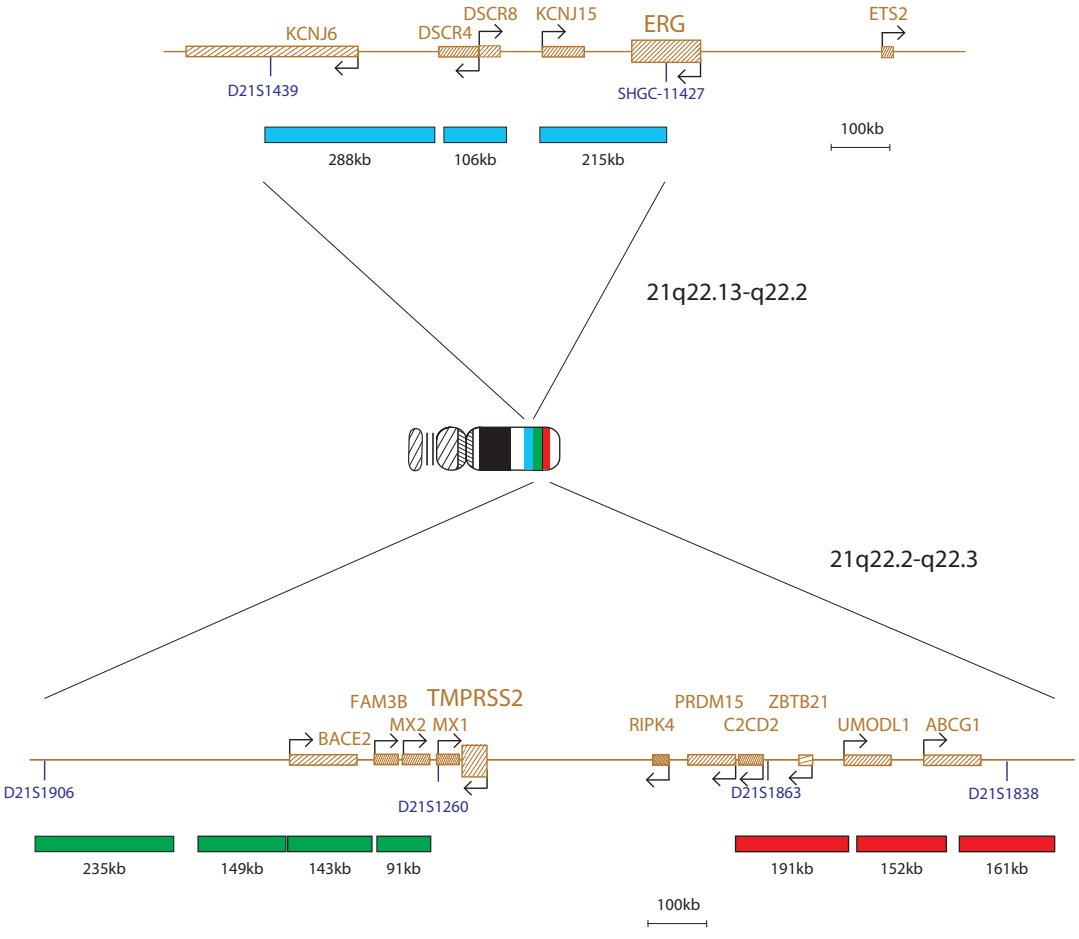


The TMPRSS2 (*transmembrane protease, serine 2*) and ERG (*v-ets avian erythroblastosis virus E26 oncogene homolog*) genes are located at 21q22.

Approximately 50% of prostate tumours show an intrachromosomal deletion of 3Mb on chromosome 21 that fuses the TMPRSS2 gene to the ERG gene[1]. This rearrangement places ERG, a member of the ETS (*erythroblast transformation-specific*) family of transcription factors, under the androgen-regulated transcriptional control of TMPRSS[2]. In approximately 2-8% of prostate cancers the TMPRSS2 gene is fused with a different partner gene from the ETS family, for example ETV1, ETV4 or ETV5[3]. The presence of a TMPRSS2-ETS fusion has been associated with an aggressive disease phenotype in prostate cancer[4].

REFERENCES

1. Saramaki *et al*., Clin Cancer Res 2008;14(11):3395-3400
2. Lapointe *et al*., Modern Pathology 2007;20(4):467-473
3. Mehra, *et al*., 2007. Modern pathology 20(5):538-44
4. Hägglöf, *et al*., 2014 PloS one, 9(2), p.e86824

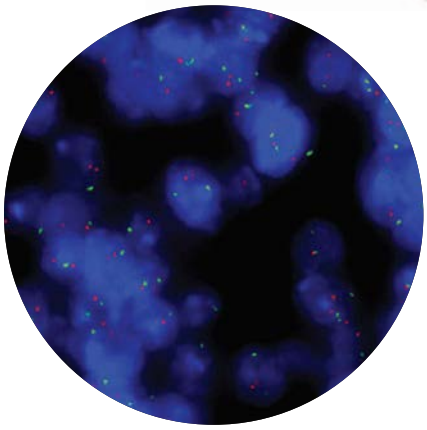


Cytocell an OGT company aquarius

Cat. No. **LPS 002-S** (5 tests)

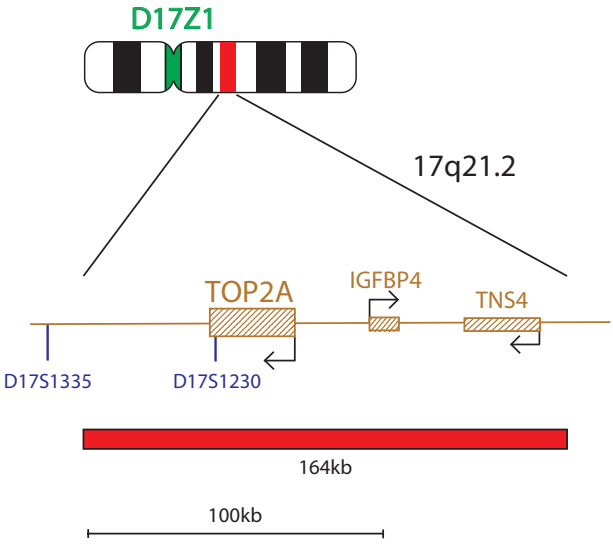
Cat. No. **LPS 002** (10 tests)

TOP2A Amplification/Deletion



The TOP2A (*topoisomerase (DNA) II alpha*) gene at 17q21.2, is located near the ERBB2 oncogene. The TOP2A encoded protein has a function in DNA replication and the transcription of mRNA[1,2]. Amplification of TOP2A gene is seen in breast cancer, frequently with co-amplification of ERBB2[3,4].

In breast cancer, TOP2A gene aberrations are a marker of response to anthracycline-based chemotherapy[5], whilst in epithelial ovarian cancers, TOP2A gain is reported to predict response to pegylated liposomal doxorubicin[6].



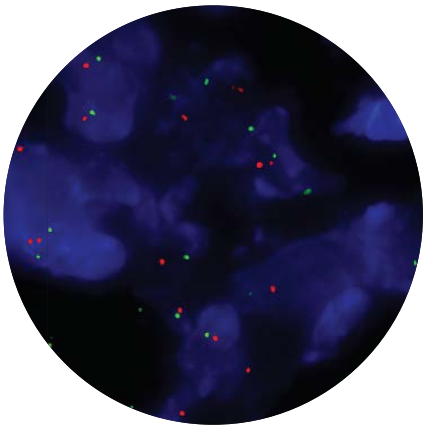
REFERENCES

1. Chen AY, Liu LF, Ann Rev Pharmacol Toxicol 1994;34:191-218
2. Tsai-Pflugfelder M *et al*., Proc Nat Acad Sci 1988;85:7177-81
3. Bofin AM *et al*., Cytopath 2003;14(6):314-9
4. Fountzilas G *et al*., BMC Cancer 2013;13:163
5. O'Malley *et al*., J Natl Cancer Inst 2009;101(9):644-650
6. Erriquez *et al*., Gynecol Oncol. 2015;138:627-33

Cytocell an OGT company aquarius

Cat. No. **LPS 005-S** (5 tests)
Cat. No. **LPS 005** (10 tests)

ZNF217 Amplification

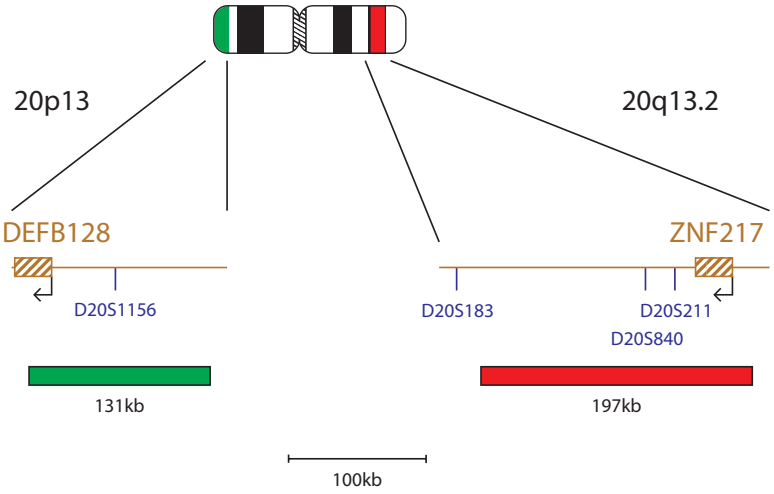


The ZNF217 (*zinc finger protein 217*) gene at 20q13.2, which functions as a transcription repressor for a variety of genes[1], is frequently amplified in human cancers[2].

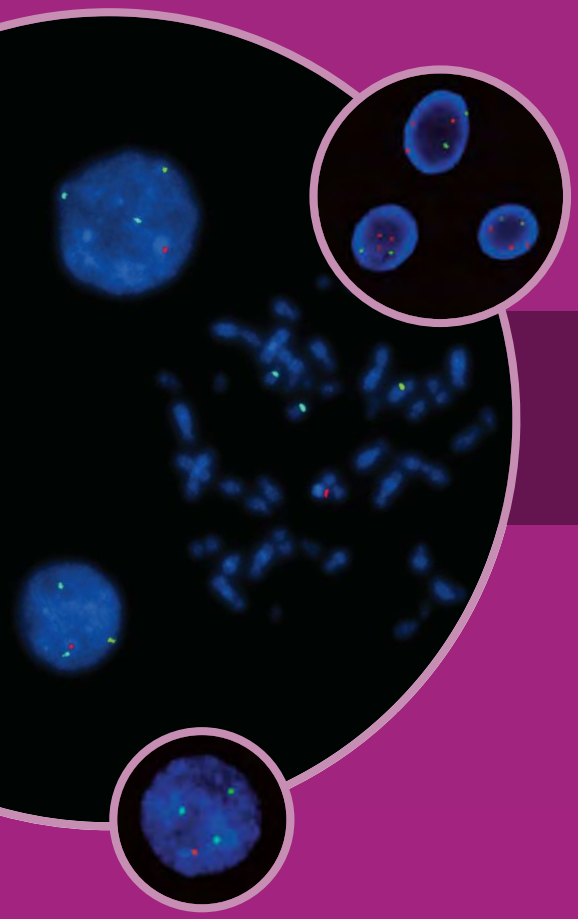
ZNF217 amplification has been reported in breast cancer[3,4], in which it has been associated with a poor prognosis[5,6]. It has also been reported in ovarian clear cell carcinoma[4,7,8] in which it correlates with shorter progression-free and overall survival[5,9]. It has been shown that the silencing of ZNF217 inhibits ovarian cancer cell growth and their invasive ability in cancer cell-lines, making it a potential target for future anti-cancer therapies[2,10].

REFERENCES

1. Quinlan KG *et al*., Mol Cell Biol 2006;26:8159-72
2. Cohen, P *et al*.,Oncotarget 2015;6:41566-41581
3. Collins C *et al*., Proc Natl Acad Sci 1998;95:8703-8
4. Yang SH *et al*., Clin Cancer Res 2005;11:612-20
5. Tanner MM *et al*., Clin Canc Res 1995;1:1455-61 7
6. Littlepage LE, *et al*., Cancer Discov. 2012;2:638-51
7. Iwabuchi H *et al*., Cancer Res 1995;55:6172-80
8. Bar-Shira A *et al*., Cancer Res 2002;62:6803-
9. Rahman MT, *et al*.,Cancer 2012;118:2846-2857
10. Sun G *et al*., Int J Oncol 2008;32:1065-71



Cytocell
an OGT company
aquarius



Prenatal

Contents

Prenatal

Cytocell's prenatal fluorescence *in situ* hybridisation (FISH) assays are designed for the rapid and accurate detection of the most common foetal chromosomal disorders.

Trisomy of chromosome 21, resulting in Down syndrome[1], is one of the most common chromosome abnormalities in humans and the risk of having an affected child is known to increase with maternal age[2]. The syndrome represents a particular combination of phenotypic findings, including characteristic facial appearance, a single palmar crease and mental retardation, and may also present with hearing and heart defects. Affected individuals show a highly increased incidence of leukaemia, particularly acute megakaryocytic leukaemia[3].

Trisomy of chromosome 18, resulting in Edwards syndrome, occurs in around 1 in 6000-8000 live births with a female sex bias[4]. The clinical findings are variable, though many exhibit growth delay, heart defects and craniofacial anomalies, as well as possible limb and kidney abnormalities[5].

The rarest trisomy, trisomy 13, responsible for Patau syndrome occurs in approximately 1 in 16,000 newborns[6]. Individuals with Patau syndrome present abnormalities affecting many parts of the body, including the heart, spinal cord, eyes, limbs, face/skull and muscles[6].

Aberrant copy numbers of the X and Y chromosomes can lead to various sex chromosome disorders, such as Klinefelter (47,XXY), Turner (45,X) and other syndromes caused by variations in copy number of X and/or Y. These syndromes have variable incidences and clinical findings[7].

Cytocell Prenatal kits contain fluorescent probes for easy identification of trisomies 21, 18 and 13 present in Down, Edwards and Patau syndrome, respectively, as well as sex chromosome aneuploidies.

REFERENCES

1. Lejeune *et al.,* C. R. Acad. Sci. 1959; 248: 1721-1722
2. Penrose *et al.,* J. Genet. 1933; 27: 219-224
3. http://www.omim.org/entry/190685
4. http://www.ojrd.com/content/7/1/81/abstract
5. Cereda and Carey. Orphanet J Rare Dis 2012; 7:81
6. http://ghr.nlm.nih.gov/condition/trisomy-13
7. Visootsak and Graham. Orphanet Journal of Rare Diseases 2006, 1:42

Cytocell an OGT company aquarius

Cat. No. **LPF 001-S** (5 tests)	Cat. No. **LPF 002-S** (5 tests)
Cat. No. **LPF 001** (10 tests)	Cat. No. **LPF 002** (10 tests)
Cat. No. **LPF 001-30** (30 tests)	Cat. No. **LPF 003-S** (5 tests)
Cat. No. **LPF 001-50** (50 tests)	Cat. No. **LPF 003** (10 tests)

Aquarius® *FAST* FISH Prenatal Kits

The Aquarius® *FAST* FISH Prenatal kit allows detection of trisomies 13, 18 and 21 (Patau, Edwards and Down syndromes) and sex chromosome aneuploidies utilising a 2 hour hybridisation protocol.

Aquarius® *FAST* FISH Prenatal kits provide the benefits of:

- 2 hour hybridisation protocol demonstrating high intensity signals and minimal background.
- Economical kit formats: 5, 10, 30** or 50** tests.
- Liquid stable reagents premixed in hybridisation solution and provided with DAPI counterstain.

Each kit contains the probe sets listed below.

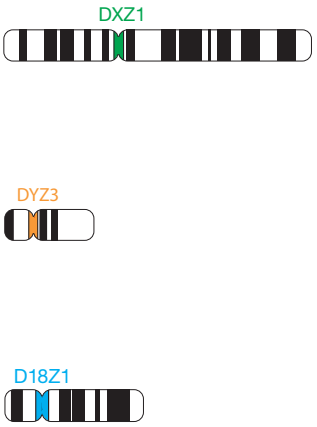
Cat. No. **LPF 001**

Probe set 1:

X centromere Xp11.1-q11.1 (DXZ1) Green

Y centromere Yp11.1-q11.1 (DYZ3) Orange

18 centromere 18p11.1-q11.1 (D18Z1) Blue



Probe set 2:

13 unique sequence (13q14.2) Green

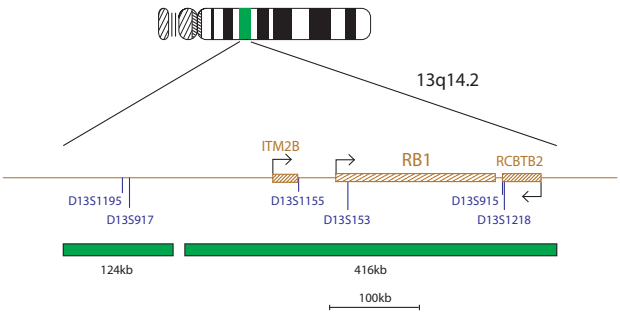
21 unique sequence (21q22.13) Orange

Cat. No. **LPF 002**

X centromere Xp11.1-q11.1 (DXZ1) Green

Y centromere Yp11.1-q11.1 (DYZ3) Orange

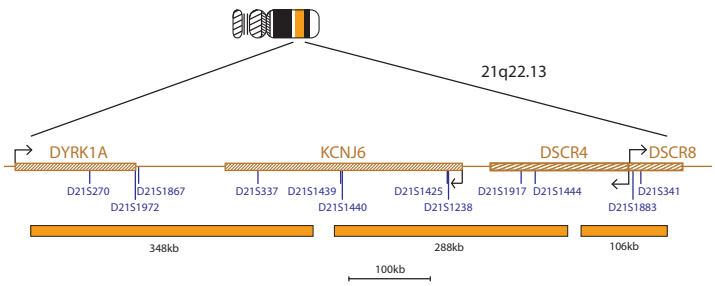
18 centromere 18p11.1-q11.1 (D18Z1) Blue



Cat. No. **LPF 003**

13 unique sequence (13q14.2) Green

21 unique sequence (21q22.13) Orange



**Not available for LPF002 and LPF003.

Cytocell an OGT company aquarius

Cat. No. **LPA 001-S** (5 tests)
Cat. No. **LPA 001** (10 tests)
Cat. No. **LPA 001-30** (30 tests)
Cat. No. **LPA 001-50** (50 tests)
Cat. No. **LPA 002** (10 tests)*
Cat. No. **LPA 003** (10 tests)*
Cat. No. **LPA 004** (10 tests)*
Cat. No. **LPA 005** (10 tests)*

Aquarius® Prenatal Enumeration Kits

The Aquarius® Prenatal Enumeration range allows detection of trisomies 13, 18 and 21 (Patau, Edwards and Down syndromes) and sex chromosome aneuploidies utilising an overnight hybridisation protocol.

Aquarius® Prenatal kits provide the benefits of:

- Overnight hybridisation protocol demonstrating high intensity signals and minimal background.
- Economical kit formats: 5, 10, 30** or 50** tests.
- Liquid stable reagents premixed in hybridisation solution and provided with DAPI counterstain.

Each kit contains the probe sets listed below.

Cat. No. **LPA 001**

Probe set 1:

X centromere Xp11.1-q11.1 (DXZ1) Green

Y centromere Yp11.1-q11.1 (DYZ3) Orange

18 centromere 18p11.1-q11.1 (D18Z1) Blue

Probe set 2:

13 unique sequence (13q14.2) Green

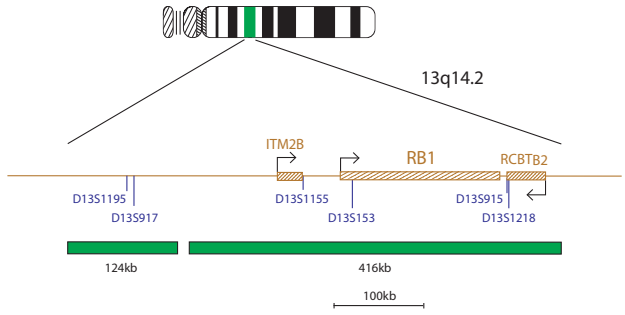
21 unique sequence (21q22.13) Orange

Cat. No. **LPA 002**

X centromere Xp11.1-q11.1 (DXZ1) Green

Y centromere Yp11.1-q11.1 (DYZ3) Orange

18 centromere 18p11.1-q11.1 (D18Z1) Blue



Cat. No. **LPA 003**

13 unique sequence (13q14.2) Green

21 unique sequence (21q22.13) Orange

Cat. No. **LPA 004**

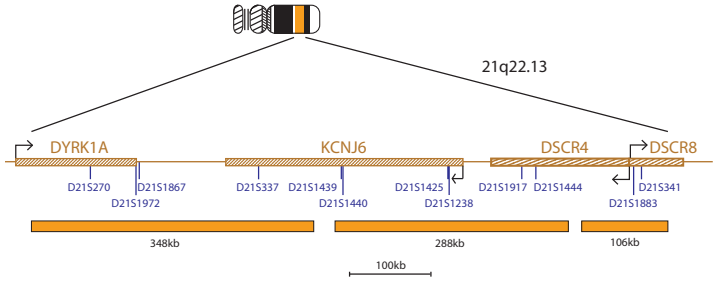
18 centromere 18p11.1-q11.1 (D18Z1) Blue

Cat. No. **LPA 005**

13 unique sequence (13q14.2) Green

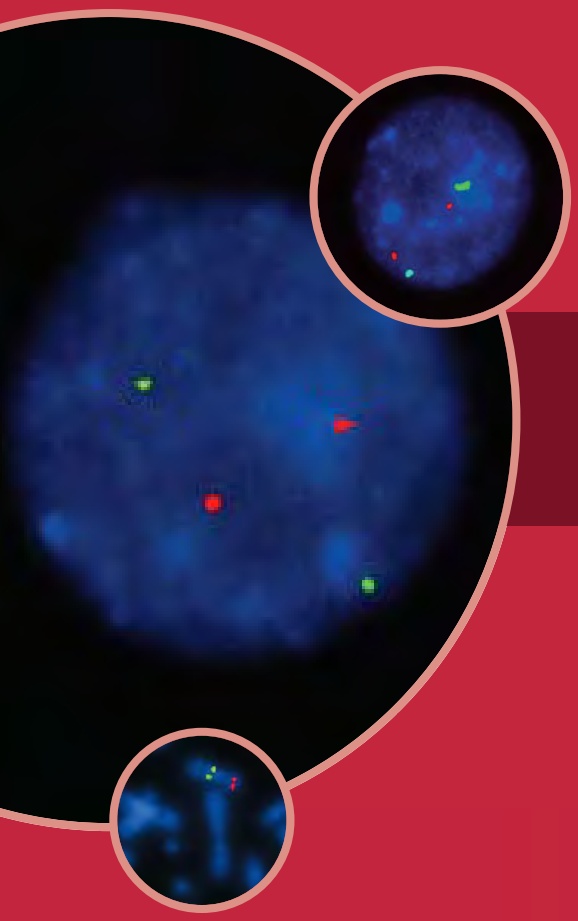
18 centromere 18p11.1-q11.1 (D18Z1) Blue

21 unique sequence (21q22.13) Orange



* Also available as 5 tests
**Not available for LPA002, 003, 004 or 005.

Cytocell
an OGT company
aquarius



Microdeletion

Contents

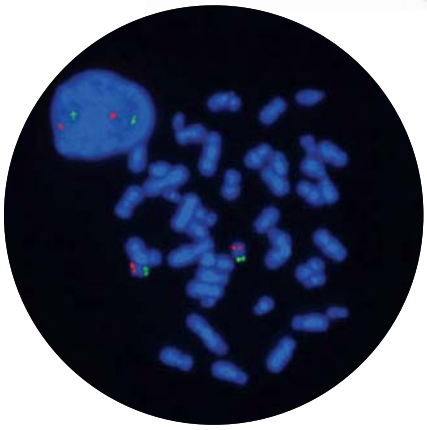
Microdeletion

Microdeletion syndromes are a group of clinically-recognisable disorders brought about by the deletion of specific regions of chromosomal DNA, causing haploinsufficiencies of important genes.

These deletions are difficult to visualise using standard cytogenetic techniques, however fluorescence *in situ* hybridisation (FISH) can resolve these submicroscopic deletions.

Cytocell's comprehensive range of Microdeletion probes features products for some of the rarest human genetic syndromes. With this in mind, we offer all Microdeletion probes in economical five, or standard ten, test kits.

Alagille (JAG1)



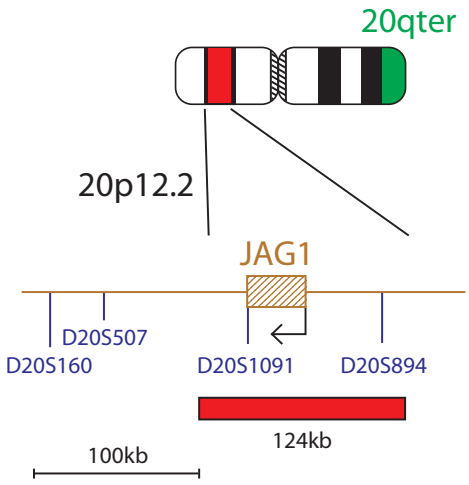
Alagille syndrome (ALGS) is an autosomal dominant disorder (with reduced penetrance) characterised by abnormalities of the liver, heart, skeleton, eye and face[1,2].

Mutations or deletions of the 36kb long human gene Jagged1 (JAG1), located on chromosome 20p12, have been identified as causal for the abnormalities found in patients with ALGS[3].

This gene encodes a ligand for the Notch 1 transmembrane receptor, which plays a key role in cell fate determination and differentiation[3,4]. The syndrome has also been noted in a patient with a deletion larger than 3Mb, including JAG1, associated with a translocation t(3;20)(q13.3;p12.2)[4].

REFERENCES

1. Alagille D *et al.,* J Pediatr 1987;110:195-200
2. OMIM entry# 118450: http://www.omim.org/entry/118450
3. Oda T *et al.,* Nature Genet 1997;16:235-42
4. Oda T *et al.,* Human Mutat 2000;16:92

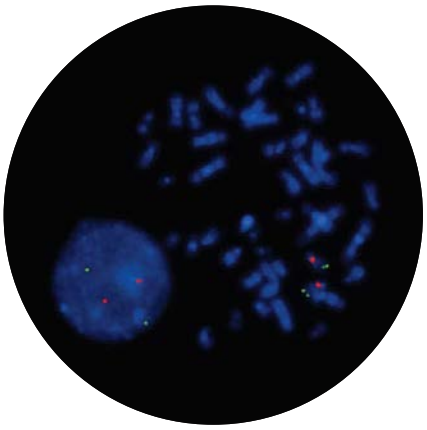


Cytocell an OGT company aquarius

Cat. No. **LPU 006-S** (5 tests)

Cat. No. **LPU 006** (10 tests)

Angelman (UBE3A/D15S10)



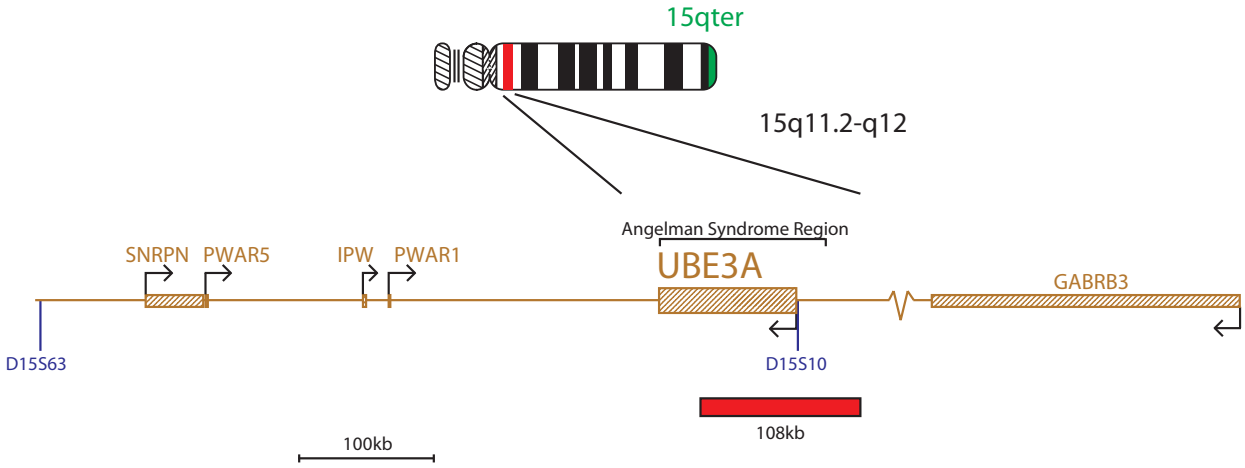
In 70% of patients with Angelman syndrome (AS), a large *de novo* maternal deletion of3-4Mb at 15q11.2-q13 is observed[1,2,3]. The remaining 30% of cases have underlying causes such as paternal uniparental disomy of the same region (~2%), imprinting defects (~2-3%) and mutations of the UBE3A gene[1].

The UBE3A gene lies within the minimum AS critical region[4] approximately 400kb telomeric to the SNRPN gene. It shows preferential expression of the maternal allele in the brain[5] and is mutated in 20-30% of AS patients with normal methylation and biparental contribution of 15q11-13. It is considered to be one of the causative AS genes[4,5].

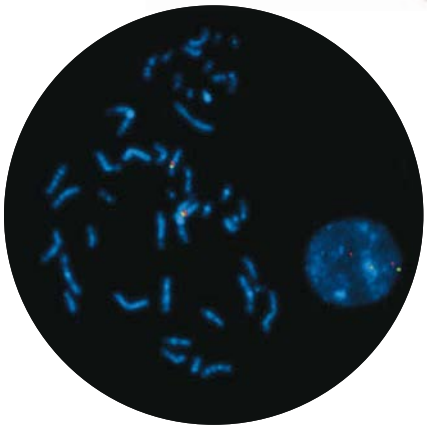
The Angelman region probe covers approximately 108kb of genomic DNA, targets most of the UBE3A gene and includes the D15S10 locus. This probe may be used to identify deletions of the AS region, though it will not detect small intragenic deletions or mutations of UBE3A. The probe may also be used to help determine the nature of a Prader-Willi syndrome deletion detected with the SNRPN/Imprinting Centre probe (see LPU005). Large, 3-4Mb deletions of 15q11-13 will cause the deletion of both probe regions (SNRPN/IC and UBE3A/D15S10). Smaller deletions incorporating the IC and SNRPN, will not cause deletion of the UBE3A/D15S10 probe. These deletions may indicate a much higher risk of recurrence (possibly via grandmatrilineal inheritance) and carriers, and their families, may require further investigation[6].

REFERENCES

1. OMIM entry #105830 http://www.omim.org/entry/105830
2. Butler MG, Am J Med Genet 1990;35:319-32
3. Clayton-Smith J, Pembrey M, E J Med Genet 1992;29:412-5
4. Sutcliffe JS et al., Genome Res 1997;7:368-77
5. Rougeulle C, Lalande M, Neurogenetics 1998;1:229-37
6. Ming et al., Am. J. Med. Genet. 92: 19-24, 2000



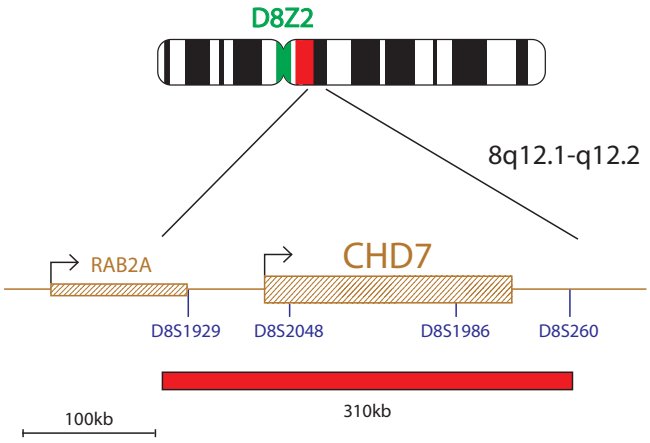
CHARGE



CHARGE syndrome is an autosomal dominant disorder that occurs in approximately 1 in 12,000 births[1].

The acronym CHARGE summarises six main clinical features: ocular Coloboma, Heart defects of any type, Atresia of the choaneae, Retardation, Genital and Ear anomalies[2].

Errors in the chromodomain 7 (CHD7) gene were identified as being causative for the syndrome in around 60% of patients with a clinical diagnosis of CHARGE[3]. CHD7 is located in 8q12.1-q12.2 and is 189kb in size. The CHD7 protein plays a role in chromatin organisation and is a member of the chromodomain helicase DNA-binding (CHD) proteins. CHD7 has an important function in early embryonic development and is ubiquitously expressed in several foetal and adult tissues, including those affected in CHARGE syndrome[3]. Most CHD7 mutations are truncating, leading to haploinsufficiency, and are generally *de novo*[3,4]. Microdeletions (or microduplications) have been proposed to account for up to 10% of CHARGE patients[5].



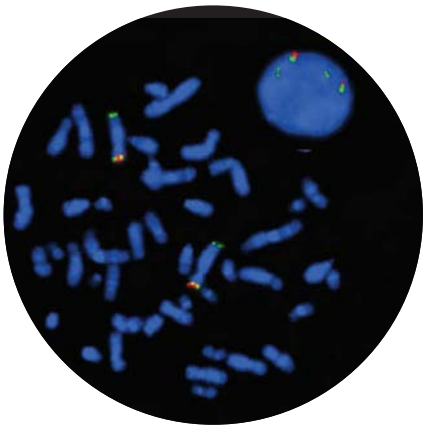
REFERENCES

1. Kallen et al., Teratology 1999: 60: 334-343
2. Pagon RA et al., J Pediat 1981;99:223-7
3. Vissers LE et al., Nat Genet 2004;36:955-7
4. Jongmans MC et al., J Med Genet 2005;43:306-14
5. Bergman et al., Eur J Med Genet. 2008; 51(5):417-25

Cytocell an OGT company aquarius

Cat. No. **LPU 013-S** (5 tests)
Cat. No. **LPU 013** (10 tests)

Cri-du-chat and Sotos Probe Combination



Cri-du-chat syndrome consists of multiple congenital anomalies, mental retardation, microcephaly, abnormal face and a mewing cry in infants. Cri-du-chat syndrome is associated with deletions, which vary in size, of part of the short arm of chromosome 5[1].

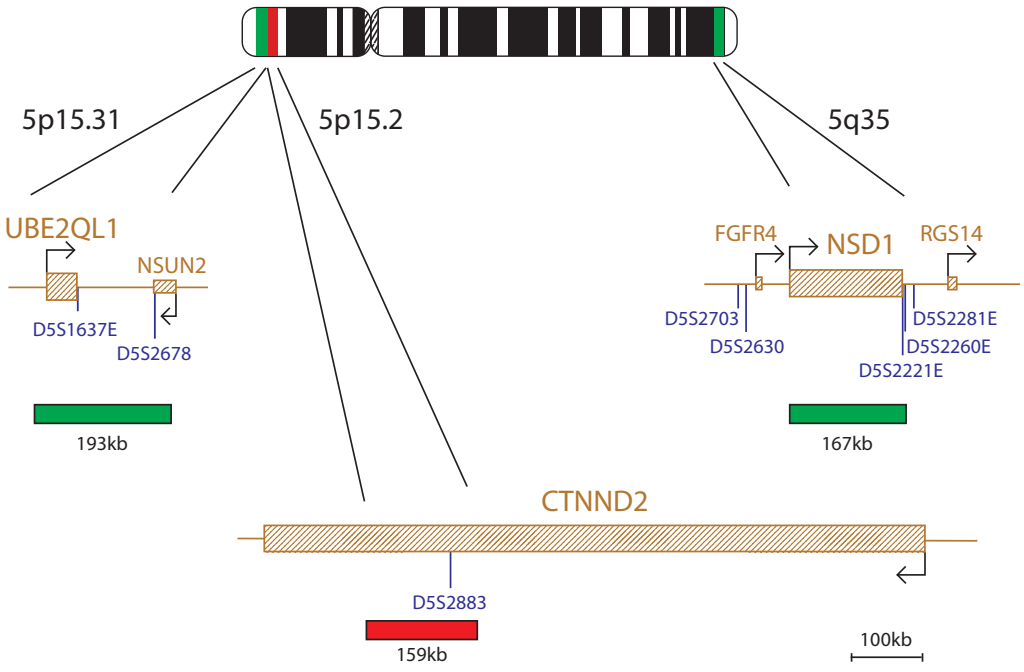
The estimated prevalence varies between 1 in 20,000 to 1 in 50,000 births[2], making it one of the more common deletion syndromes. A critical chromosomal region involved in the high-pitched cry has been mapped to the proximal part of chromosome band 5p15.3[3]. The region involved in the remaining features of the syndrome has been mapped to 5p15.2[3,4,5].

Sotos syndrome-1 (SOTOS1) is a neurological disorder characterised by a distinctive facial appearance, overgrowth in childhood and developmental delay[6]. Malignant tumour formation has also been reportedly associated with SOTOS1[7].

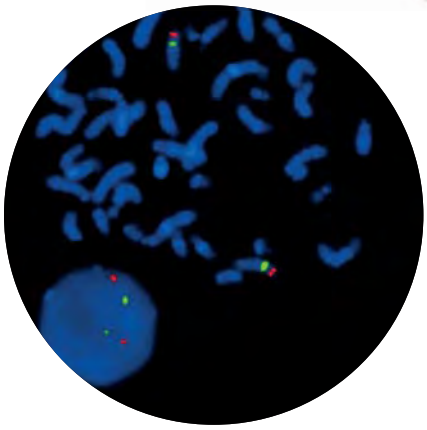
NSD1, a gene encoding a histone methyltransferase, and implicated in chromatin regulation[8], was identified as the gene disrupted by the 5q35 breakpoint in a patient carrying a chromosomal translocation[9]. The major causes of SOTOS1 are mutations of the NSD1 gene or deletions of the 5q35 region causing haploinsufficiency of the NSD1 gene.

REFERENCES

1. Lejeune J *et al.,* C R Hebd Seances Acad Sci 1963;257:3098-102
2. Niebuhr E *et al.,* Hum Genet 1978;44:227-75
3. Mainardi PC *et al.,* J Med Genet 2001;38:151-8
4. Overhauser J *et al.,* Hum Mol Genet 1994;3:247-52
5. Wu Q *et al.,* Eur J Hum Genet 2005;13:475-85
6. Cole TR and Hughes HE, J Med Genet 1994;31(1):20-32
7. Maldonado V *et al.,* Am J Dis Child 1984;138:486-8
8. Tatton-Brown K and Rahman N, Eur J Hum Genet 2007;15:264-71
9. Kurotaki N *et al.,* Nat Genet 2002;30:365-6

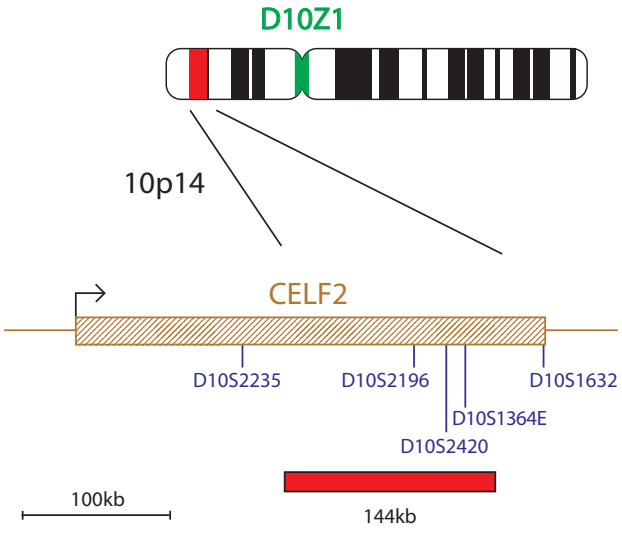


DiGeorge II (10p14)



DiGeorge syndrome[1], and a variety of congenital malformation syndromes including velocardiofacial syndrome (VCFS)[2], share the deletion of chromosome 22 at 22q11.2[2,3,4,5]. These chromosome 22 deletions are collectively coined CATCH22, a mnemonic that covers the clinical findings of Cardiac abnormality, Abnormal facies, Thymic aplasia, Cleft palate and Hypocalaemia/Hyperthyroidism due to a chromosome 22 deletion. In DiGeorge syndrome, however, cases have also been found in which patients have a deletion on chromosome 10p13.4 (DGS2) instead of chromosome 22[6,7,8].

The deletion of the DGS2 locus on 10p may be 50 times less frequent than that of the DGS1 locus on 22q and has been estimated to occur in 1 in 200,000 live births[9]. The CELF2 gene has been identified within the 300kb minimally deleted region of DGS2 and is postulated to be involved in the DGS2 deletion[10]. CELF2 is a candidate gene for the heart defect and thymus hypoplasia/aplasia associated with partial monosomy 10p[10] and may be involved in atrial septal defects (ASDs), a common cardiac anomaly associated with DGS2[11].



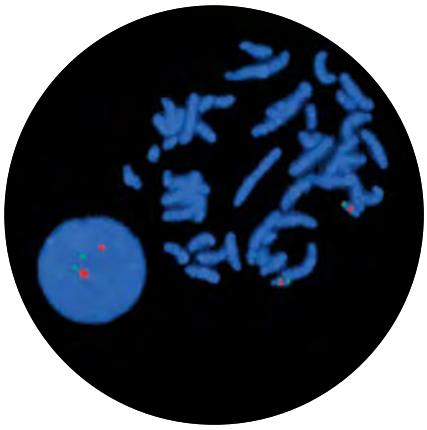
REFERENCES

1. DiGeorge AM, J Pediatr 1965;67:907
2. Shprintzen RJ *et al.,* Cleft Palate J 1978;15:56-62
3. Wilson DI *et al.,* J Med Genet 1993;30:852-6
4. Driscoll DA *et al.,* J Med Genet 1992;50:924-33
5. Burn J *et al.,* J Med Genet 1993;30:822-4
6. Schuffenhauer S *et al.,* Ann Genet 1995;38(3):162-7
7. Daw SC *et al.,* Nat Genet 1996;13:458-60
8. Dasouki M *et al.,* Am J Med Genet 1997;73(1):72-5
9. Berend SA *et al.,* Am J Med Genet 2000;91(4):313-7
10. Lichtner P *et al.,* J Mol Med 2002;80:431-42
11. Yatsenko SA *et al.,* Clin Genet 2004;66:128-36

Cytocell an OGT company aquarius

Cat. No. **LPU 004-S** (5 tests)
Cat. No. **LPU 004** (10 tests)

DiGeorge and 22q13.3 Deletion Syndrome Probe Combinations



DiGeorge syndrome

DiGeorge syndrome[1], and a variety of congenital malformation syndromes including velocardiofacial syndrome (VCFS)[2], have in common deletions of chromosome 22 at 22q11.2[2,3,4,5]. These syndomic phenotypes are collectively coined CATCH22, a mnemonic that covers the clinical findings of Cardiac abnormality, Abnormal facies, Thymic aplasia, Cleft palate and Hypocalaemia/Hyperthyroidism due to a chromosome 22 deletion.

In addition, around 29% of nonsyndromic patients with isolated conotruncal defects have been shown to have a 22q11.2 microdeletion[6]. The incidence of these anomalies is estimated to be 1:4000 to 1:9700 live births[7]; therefore deletion of 22q11.2 represent one of the most common genetic defects.

A region of approximately 2Mb, referred to as the DiGeorge Critical Region (DGCR), is the most commonly deleted region and occurs in up to 90% of patients with DiGeorge Syndrome[5,8,9]. Within the DGCR, a minimal critical region of 300-480kb has been described[10,11], containing several genes, including HIRA (TUPLE1), TBX1, SLC25A1 (CTP) and CLTD.

22q13.3 Deletion Syndrome

The 22q13.3 deletion syndrome presents a recognisable phenotype characterised by hypotonia, delay or absence of expressive speech, global developmental delay, normal to accelerated growth and mild dysmorphic features[12,13].

Some deletions of the terminal region of chromosome 22q are cytogenetically visible. However, a few cases of cryptic deletions have been reported[12,14], suggesting that the actual incidence of 22q telomere deletion may be higher than previously thought.

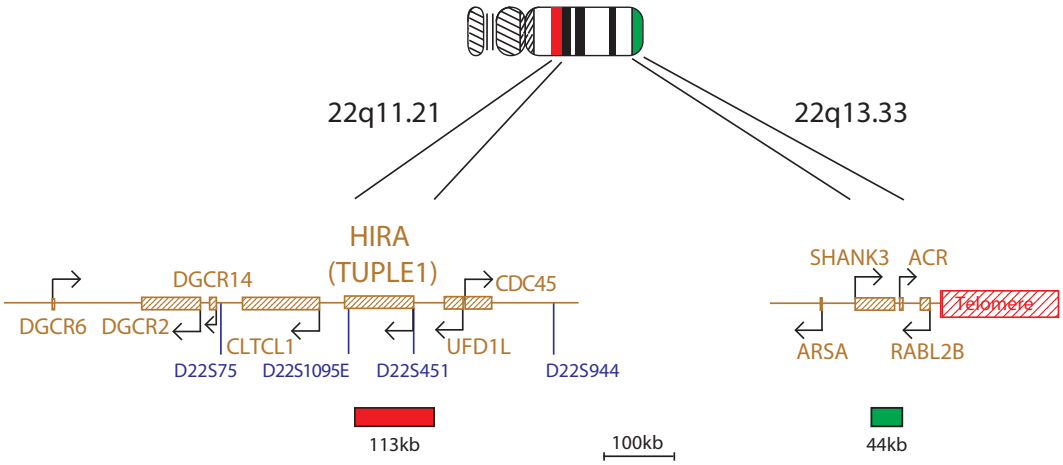
Several observations of patients with 22q13.3 deletion showed that the SHANK3 (ProSAP2)[20] gene, encoding a structural protein of the postsynaptic density of excitation synapses and expressed in the cortex and cerebellum of the brain[15], was disrupted[15,16,17] or deleted[18], making it a candidate causative gene for this syndrome. The deletion varies dramatically in size from 130kb to 9Mb[18,19,20]. The use of 22q subtelomeric probes, distal to the ARSA gene, have therefore been recommended for examining all 22q13.3 deletions[20,21].

REFERENCES

1. Pinsky L, DiGeorge AM, J Pediatr 1965;66:1049-54
2. Shprintzen RJ et al., Cleft Palate J 1978;15:56-62
3. Burn J et al., J Med Genet 1993;30:822-4
4. Wilson DI et al., J Med Genet 1993;30:852-6
5. Driscoll DA et al., J Am Hum Genet 1992;50:924-33
6. Goldmuntz E et al., J Med Genet 1993;30:807-12
7. Tezenas Du Montcel S et al., J Med Genet 1996;33:719
8. Driscoll DA et al., Am J Med Genet 1992;44(2):261-8
9. Scambler PJ et al., Genomics 1991;10:201-6
10. Halford S et al., Hum Mol Genet 1993;2(12):2099-107
11. Carlson C et al., Am J Hum Genet 1997;61:620-9
12. Phelan MC et al., Am J Med Genet 2001;101(2):91-9
13. Phelan MC. Orphanet Journal of Rare Diseases 2008, 3:14
14. Prasad C et al., Clin Genet 2000;57(2):103-9
15. Beeckers TM et al., J Neurochem 2002;81(5):903-10
16. Bonaglia MC et al., Am J Hum Genet 2001;69(2):261-8
17. Anderlid BM et al., Hum Genet 2002;110(5):439-43
18. Wilson HL et al., J Med Genet 2003;40(8):575-84
19. Dupont C et al., French Speaking Cytogeneticists Association Congress 2003
20. Luciani J et al., J Med Genet 2003;40(9):690-6
21. Chen CP et al., Prenat Diagn 2003;23(6):504-8

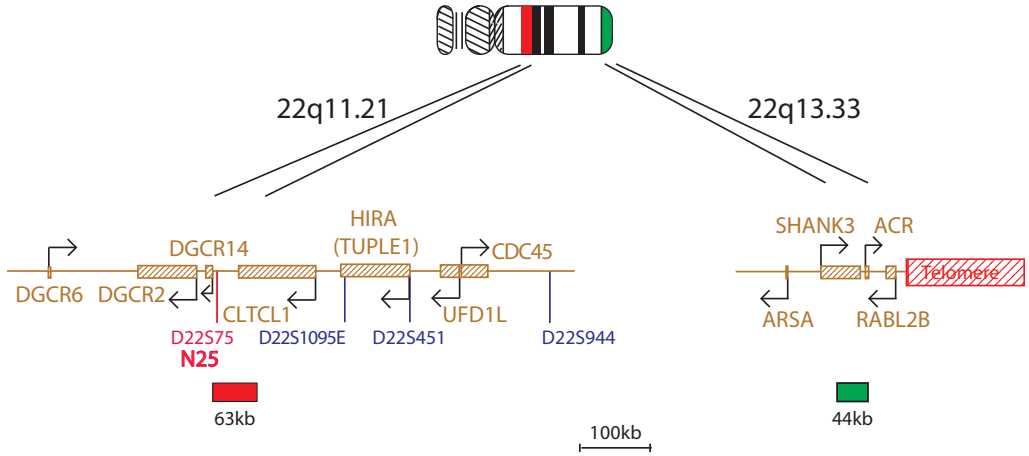
VCFS TUPLE 1

Cat. No. **LPU 004**



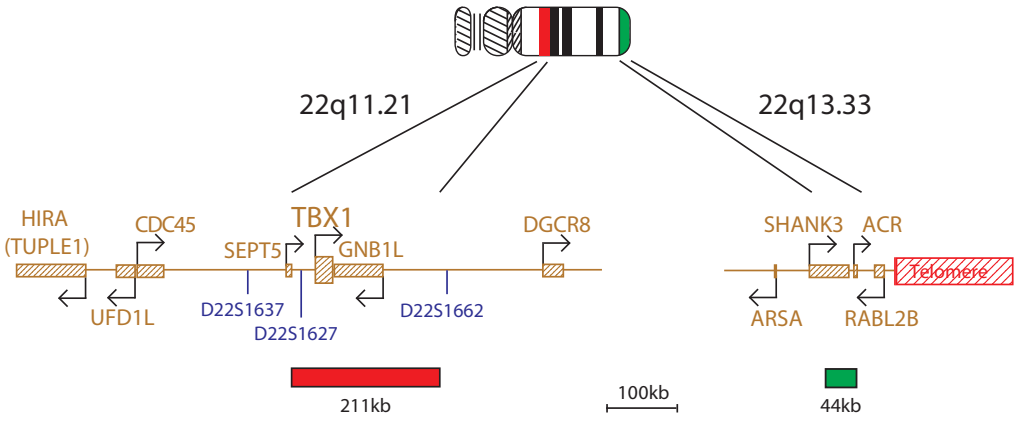
VCFS N25

Cat. No. **LPU 010**



TBX1

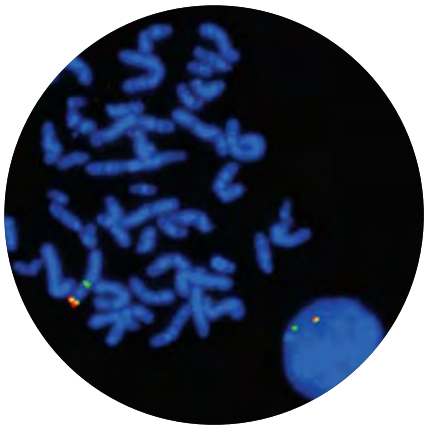
Cat. No. **LPU 014**



Cytocell an OGT company aquarius

Cat. No. **LPU 016-S** (5 tests)
Cat. No. **LPU 016** (10 tests)

Kallmann (KAL1) and Steroid Sulphatase Deficiency (STS) Probe Combination



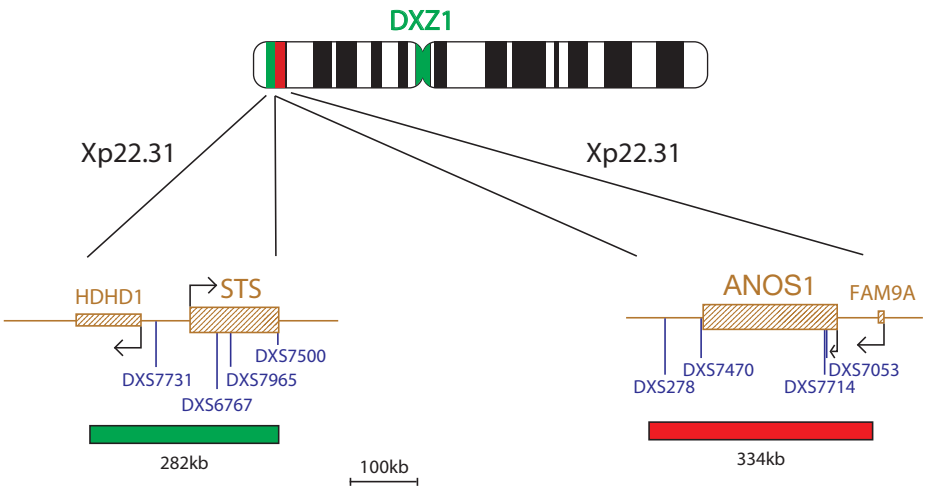
Kallmann syndrome (KS) is a developmental disease characterised by olfactory deficiency[3] and hypogonadotrophic hypogonadism (HH), which is responsible for the absence of spontaneous puberty[1].

Kallmann syndrome is a heterogeneous developmental genetic disorder affecting approximately 1 in 8,000 males and 1 in 40,000 females[2]. Reports indicate three modes of inheritance: X-linked, autosomal dominant and autosomal recessive[1,4].

It has been shown that mutations in the ANOS1 (KAL1) gene at Xp22.3 result in the X-linked form of KS[5]. ANOS1 consists of 14 exons and extends over 200kb and abnormalities of ANOS1 reported in patients with KS include missense and nonsense mutations, splice site mutations, intragenic deletions and submicroscopic chromosomal deletions involving the entire ANOS1 gene[7].

Steroid Sulphatase Deficiency (STS) (also known as X-linked Ichthyosis)[8] is the second most common type of ichthyosis and one of the most frequent human enzyme deficiency disorders.

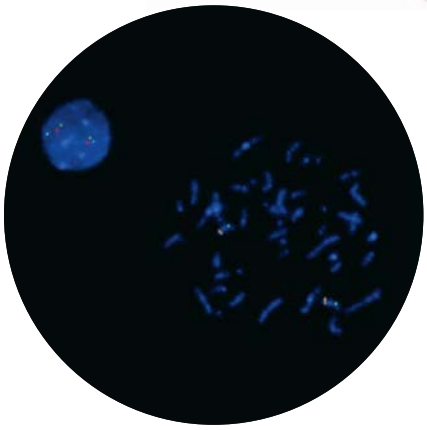
Deficiency of the STS enzyme is known to be responsible for dark, adhesive and regular scaling of the skin[9]. The gene encoding this protein maps to the distal short arm of chromosome X, which escapesX-chromosome inactivation and has the highest ratio of chromosomal deletions among all genetic disorders[10]. Complete deletions of the STS gene have been found in more than 90% of patients[11]. The deletions can extend to involve neighbouring genes, causing contiguous gene defects. Therefore, STS may be associated with KS[12].



REFERENCES

1. Kallmann FJ *et al.,* Am J Ment Defic 1944;48:203-36
2. Hu Y *et al.,* Int J Biochem Cell Biol 2003;35:1157-62
3. Hockaday TD, Postgrad Med J 1966;42:572-4
4. White BJ, Am J Med Genet 1983;15:417-35
5. Hardelin JP *et al.,* Human Mol Genet 1993;2:373-7
6. Del Castillo I *et al.,* Nat Genet 1992;2:305-10
7. Izumi Y *et al.,* Endocr J 2001;48:143-9
8. Wells RS *et al.,* Arch Dermatol 1965;92(1):1-6
9. Valdes-Flores M *et al.,* J Invest Dermatol. 2001;116(3):456-8
10. Hernandez-Martin A *et al.,* Br J Dermatol 1999;141(4):617-27
11. Hazan C *et al.,* Dermatology Online 2005;11(4):12
12. Paige DG *et al.,* Br J Dermatol 1994;131(5):622-9

Langer-Giedion

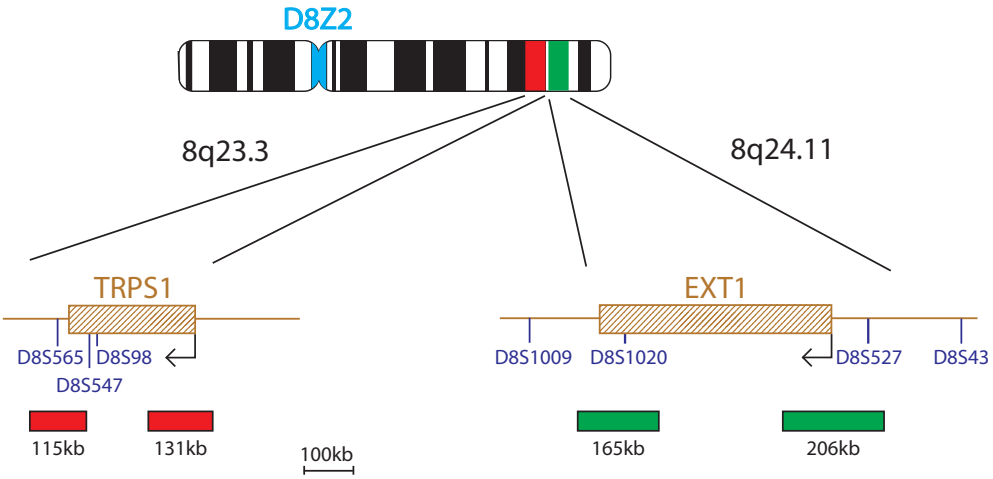


Langer-Giedion syndrome (LGS; tricho-rhino-phalangeal syndrome type II) is an autosomal dominant contiguous gene deletion syndrome involving chromosome bands 8q23.3 and 8q24.1[1].

LGS is characterised by cranio-facial and skeletal abnormalities including multiple cartilaginous exostoses and cone-shaped epiphyses. Mental retardation is also a common finding. LGS combines the clinical features of two autosomal dominant diseases: tricho-rhino-phalangeal syndrome type 1 and multiple cartilaginous exostoses (caused by defects in the TRPS1 and EXT1 genes respectively). Both genes involved in these conditions are within the Langer-Giedion deletion region, though TRPS1 maps more than 1Mb proximal to EXT1[2,3].

REFERENCES

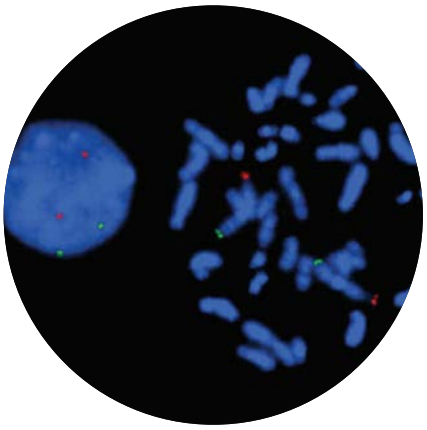
1. Buhler, Malik, Am J Med Genet 1984;19:113-9
2. Ludecke HJ *et al.*, Hum Mol Genet 1995;4:31-6
3. Hou *et al.*, Genomics 1995;29(1):87-97



Cytocell an OGT company aquarius

Cat. No. **LPU 020-S** (5 tests)
Cat. No. **LPU 020** (10 tests)

Monosomy 1p36



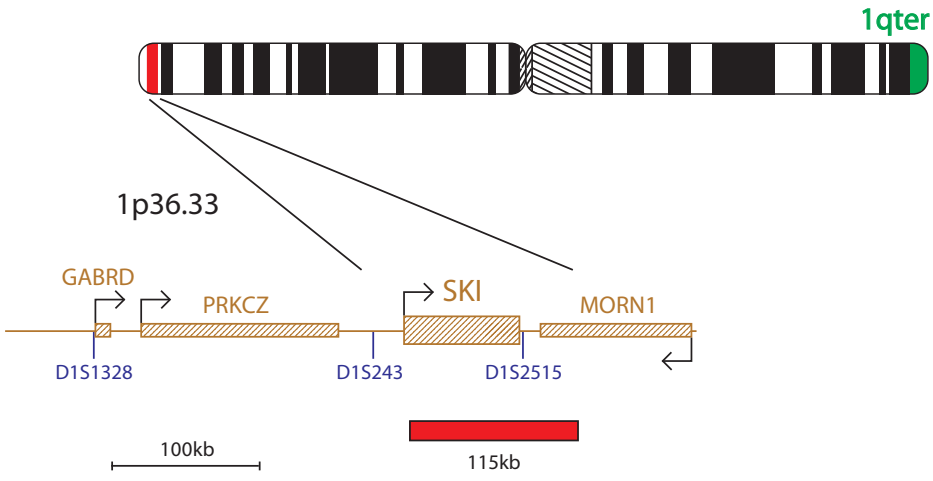
Monosomy 1p36 (1p36 deletion syndrome) is one of the most common terminal deletion syndromes, occurring in an estimated 1 in 10,000 births[1].

It is characterised by developmental delay, growth abnormalities and craniofacial dysmorphism. Minor cardiac malformations, sensorineural hearing loss and opthalmological anomalies have also been observed[2]. Deletions are extremely variable and range from 1.5 to 10.5Mb[3].

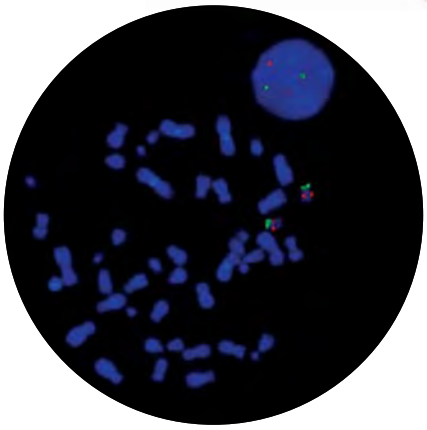
The SKI gene, located at 1p36.33, was deleted in all individuals tested with 1p36 deletion syndrome[4]. This gene is involved in neural tube development and muscle differentiation[5] and deletions in mice produce phenotypes with some similarities to those seen in individuals with 1p36 deletion syndrome[6].

REFERENCES

1. Shaffer, Lupski *et al.,* Annu Rev Genet 2000;34:297-329
2. Slavotinek A *et al.,* J Med Genet 1999;36:657-663
3. Heilstedt HA *et al.,* Am J Hum Genet 2003;72:1200-12
4. Colmenares C, Nat Genet 2002;30:106-9
5. Kaufman CD *et al.,* Mech Dev 2000;95:147-62
6. Berk M *et al.,* Genes Dev 1997;11:2029-39

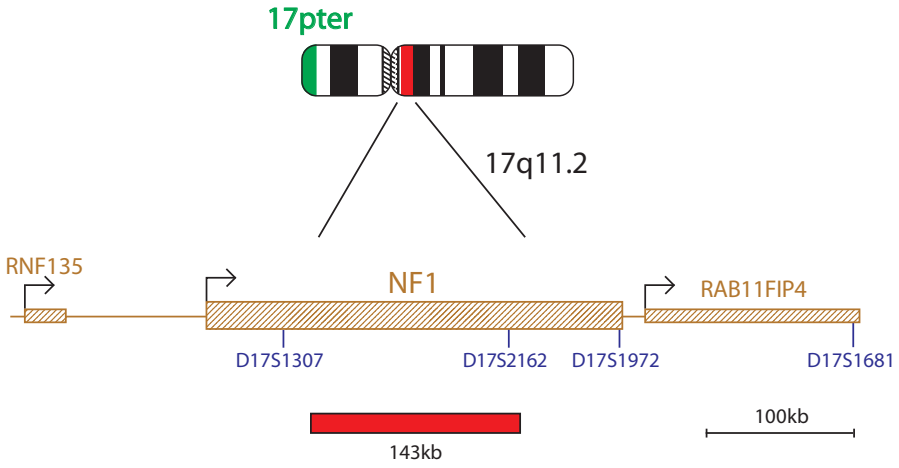


Neurofibromatosis Type 1



Neurofibromatosis type 1 (NF1) is a relatively common autosomal dominant disorder, occurring in 1 in 3,000-4,000 people[1]. It is a characterised by neurofibromas, café-au-lait spots, freckles, Lisch nodules, bone deformities, learning disabilities, macrocephaly, short stature and predisposition to developing tumours such as myeloid malignancies, gliomas and pheochromocytomas[2,3,4].

NF1 is caused by mutations of the tumour suppressor gene, Neurofibromin 1 (NF1), which spans approximately 280kb and is located at 17q11.24[5]. Mutations encompass both single nucleotide substitutions and large genomic deletions. Patients with deletions of the entire gene typically have a more severe presentation than those with intragenic mutations[6]. Approximately 5-20% of patients with NF1 carry a heterozygous deletion and thus lack one copy of the NF1 gene and further 11 or more contiguous genes[7]. There are two common sized recurrent deletions, both mediated by non-allelic homologous recombination between regions of high sequence homology: Type 1, spanning 1.4Mb between segmental duplicons and Type 2, with breakpoints in the SUZ12 gene and its pseudogene 1.2Mb away[8]. Atypical deletions have also been noted with non-recurrent breakpoints[8].



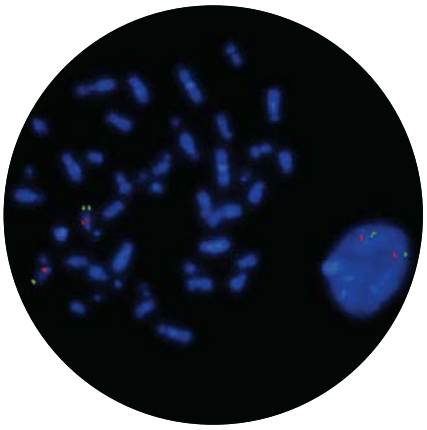
REFERENCES

1. Laycock-van Spyk S *et al.,* Human Genomics 2011; 5:623-690
2. Bader JL *et al.,* Ann N J Acad Sci 1986;486:57-65
3. Huson SM and Hughes RAC, The Neurofibromatoses: A Pathogenic and Clinical Overview. Chapman and Hall, London. 1994
4. Trovo-Marqui AB, Tajara EH *et al.,* Clin Genet 2006;70:1-13
5. Cichowski K, Jacks T *et al.,* Cell 2001;104(4):593-604
6. Pasmant E *et al.,* Hum Mutat. 2010 Jun;31(6):E1506-18
7. Jeong SY *et al.,* J Korean Med Sci. 2010 May;25(5):804-8
8. Steinmann *et al.,* Eur J Hum Genet 2008;16:572-580

Cytocell an OGT company aquarius

Cat. No. **LPU 005-S** (5 tests)
Cat. No. **LPU 005** (10 tests)

Prader-Willi/Angelman (SNRPN)

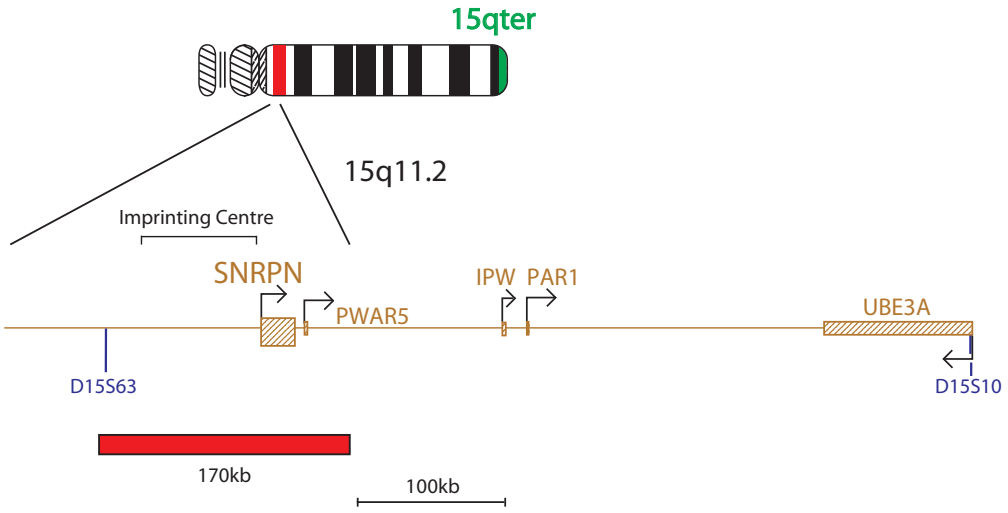


Prader-Willi Syndrome (PWS) and Angelman Syndrome (AS) are distinct neurogenetic disorders caused by the loss of function of genes on chromosome 15 (bands 15q11-13), on either the paternally or maternally inherited chromosome, respectively[1].

In 70% of patients, a large interstitial deletion of 3-4Mb is observed[1,2]. In around 3% of patients, an imprinting defect is observed, caused by either an epimutation or a microdeletion of the Imprinting Centre (IC)[1,3]. Uniparental disomy, in which both chromosome 15s are inherited from the same parent, accounts for most of the remaining patients with PWS/AS[1].

The SNRPN gene is one of four imprinted loci that are expressed from the paternal chromosome 15 region (15q11-13) and maps to the minimally deleted region (MDR) involved in PWS[5]. Its chromosomal location and imprinting status suggest it plays a possible role in the aetiology of PWS[4].

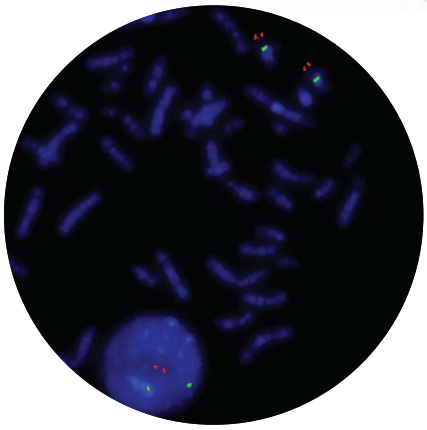
The imprinting centre (IC) maps to a 100kb region proximal to SNRPN. Parental deletions or mutations in the IC impair the imprinting process in 15q11-13 and cause one of two distinct diseases in their offspring[5,6]. Most of the PWS imprinting deletions involve SNRPN and are approximately 200kb in size. The AS imprinting deletions are small (approximately 40kb), involve the BD3 region, and do not include SNRPN.



REFERENCES

1. Butler MG. Curr Genomics. 2011 May; 12(3): 204-215
2. Clayton-Smith J and Pembrey M. J Med Genet 1992;29:412-5
3. Buiting K *et al.*, Am J Hum Genet 1998;63(1):170-80
4. Glenn C *et al.*, Am J Hum Genet 1996;58:335-46
5. Buiting K *et al.*, Nat Genet 1995;9:395-400
6. Dittrich B *et al.*, Nat Genet 1996;14:163-70

Rubinstein-Taybi

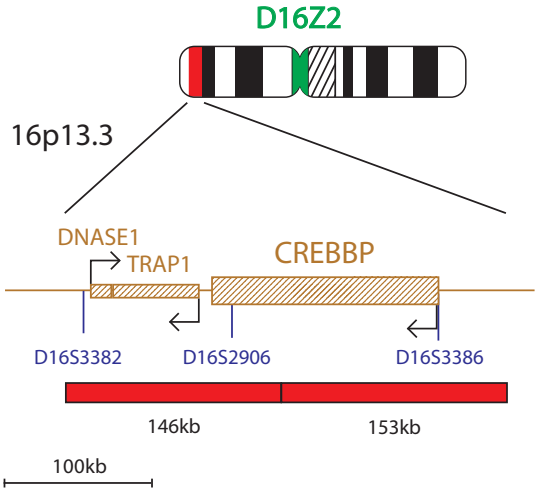


Rubinstein-Taybi is a well-defined syndrome characterised by short stature, mental retardation, facial abnormalities, and broad thumbs and first toes[1].

This condition was described in 1957[2] but a larger series of cases described in 1963 by Rubinstein and Taybi[1] led to the current syndrome name. It is an autosomal-dominant disorder with a frequency of 1 in 100,000 newborns[3]. The Rubinstein-Taybi syndrome (RTS) locus resides in chromosome band 16p13.3 and includes a gene encoding a cAMP response element binding protein (CREBBP)[4]. This gene spans approximately 150kb[4] and dosage abnormalities are the common cause of RTS[5], with microdeletions of this region accounting for 10-15% of cases[5]. Disruptions of CREBBP, by either gross chromosomal rearrangements or point mutations, have also been shown to be responsible for Rubinstein-Taybi syndrome[4,6].

REFERENCES

1. Rubinstein JH, Taybi H, Am J Dis Child 1963;105:588-608
2. Matsoukas and Theodorou Chir Orthop Reparatrice Apar Mot 1957;43:142-6
3. Jacobs *et al.,* Clin Ophthalmol. 2012; 6: 1369–1371
4. Petrij F *et al.,* J Med Genet 2000;37(3):168-76
5. Stef M *et al.,* Eur J Hum Genet 2007;15(8):843-7
6. Bartsch O *et al.,* Eur J Hum Genet 1999;7(7):748-56

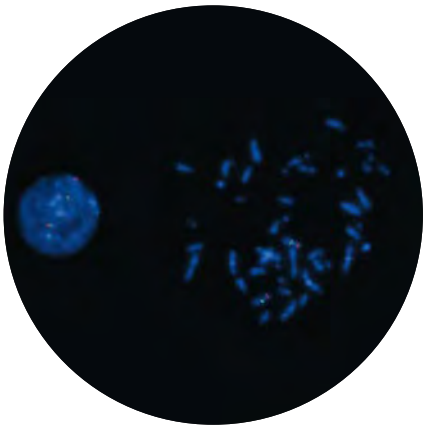


Cytocell an OGT company aquarius

Cat. No. **LPU 024-S** (5 tests)

Cat. No. **LPU 024** (10 tests)

Saethre-Chotzen/Williams-Beuren Combination



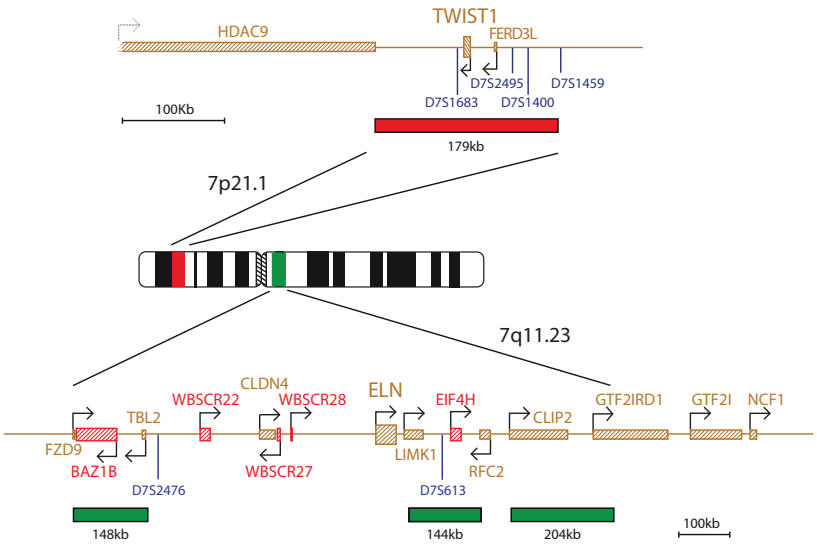
Saethre-Chotzen syndrome is a rare, congenital, autosomal dominant disorder characterised by craniofacial and limb abnormalities[1].

The incidence of this syndrome is estimated to be 1 in 25,000-50,000 live births, though due to the phenotype often being very mild, it is possible that the syndrome is under diagnosed[1]. The identification of TWIST1 (a basic helix-loop-helix transcription factor on chromosome band 7p21.1) as a causative gene[2,3] has proved invaluable for the diagnosis of this phenotypically variable disorder[1].

Williams-Beuren Syndrome (WBS) is a rare neurodevelopmental disorder caused by a deletion (approx. 1.5-1.8Mb in size, containing around 28 genes[6]) within chromosome band 7q11.23[4]. The incidence of this syndrome is estimated at 1 in 7,500 to 20,000 live births[5,6].

Patients display a distinctive 'elfin' facial appearance, connective tissue problems, SupravalVular Aortic Stenosis (SVAS), growth retardation, renal anomalies, transient hypercalcaemia, hyperacusis and mental retardation[7]. Haploinsufficiency or hemizygosity of the elastin (ELN) gene has been identified as being responsible for the SVAS[8,9] but none of the other clinical features of the syndrome have been unequivocally attributed to specific genes within the WBS deleted region. These genotype-phenotype correlations are made more difficult in WBS patients as the deletion has also been shown to have an effect on normal copy number genes that neighbour the deletion breakpoints[10].

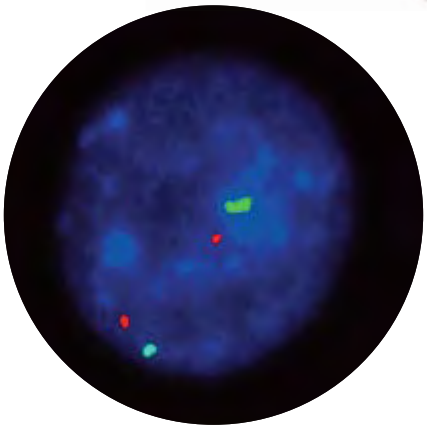
The Saethre-Chotzen/Williams-Beuren Combination contains a red probe that covers the TWIST1 gene for Saethre-Chotzen syndrome and a green probe covering the area around the ELN gene in the Williams-Beuren syndrome deleted region.



REFERENCES

1. Orphanet # ORPHA794: www.orpha.net
2. Howard TD *et al.,* Nat Genet 1997;15:36-41
3. El Ghouzzi V *et al.,* Nat Genet 1997;15:42-6
4. Francke U *et al.,* Hum Mol Genet 1999;8:1947-54
5. Stromme *et al.,* J. Child. Neurol 2002;17:269-71
6. OMIM #194050. www.omim.org/194050
7. Pober BR and Dykens EM. Child Adolesc Psychiatr Clin North Am 1996;5:929-43
8. Li DY *et al.,* Hum Mol Genet 1997;6:1021-8
9. Tassabehji M *et al.,* Hum Mol Genet 1997;6:1029-36
10. Merla *et al.,* Am J Hum Genet 2006; 79:332-341

SHOX



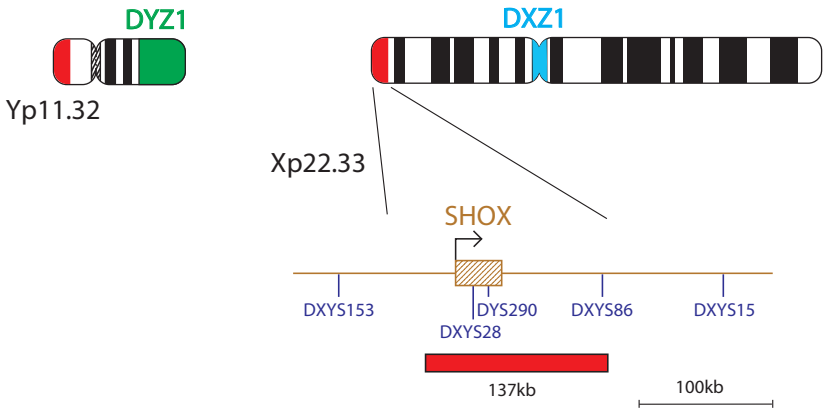
The SHOX (short stature homeobox) is located in the pseudoautosomal region (PAR1) of chromosomes X and Y, in bands Xp22.33 and Yp11.32[1].

The gene encodes a transcription factor of 292 and 225 amino acids (SHOXa and SHOXb respectively), whose translated proteins differ in the C-terminal regions. SHOX is a cell-specific homeodomain protein involved in cell cycle and growth regulation and activates transcription in osteogenic cells[2]. SHOX haploinsufficiency is involved in the aetiology of idiopathic short stature and the short stature observed in Turner syndrome[3]. Homozygous loss of the SHOX gene has been correlated with Langer type mesomelic dysplasia. Subsequently, heterozygous SHOX mutations were also shown to cause Leri-Weill dyschondrosteosis[4].

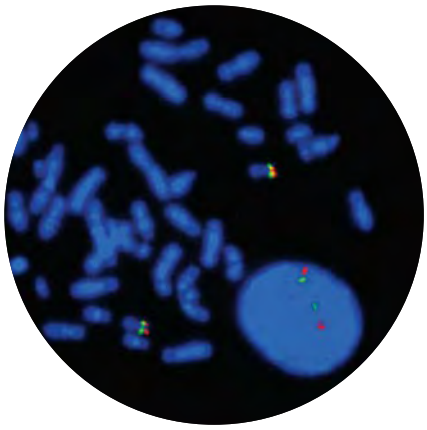
The incidence of SHOX deficiency is between 1 in 2000 and 1 in 5000 in the general population and between 1 in 40 and 1 in 150 in patients with idiopathic short stature[5,6].

REFERENCES

1. Rao E *et al.*, Nat Genet 1997;16:54-63
2. Rao E *et al.*, Hum Mol Genet 2001;10:3083-91
3. Clement-Jones M *et al.*, Hum Mol Genet. 2000 Mar 22;9(5):695-702
4. Robertson S *et al.*, J Med Genet. 2000 Dec;37(12):959-64
5. Leka SK *et al.*, Hormones 2006;5:107-18
6. Jorge AL *et al.*, Clin Endocri 2007;66:130-5



Smith-Magenis (RAI1 and FLII)/Miller-Dieker Probe Combinations



Smith-Magenis syndrome (SMS) is a multiple congenital anomaly syndrome characterised by mental retardation, neurobehavorial abnormalities, sleep disturbances, short stature, minor craniofacial and skeletal anomalies, congenital heart defects and renal anomalies[1,2].

It is one of the most frequently observed human microdeletion syndromes and is associated with an interstitial deletion of the chromosome band 17p11.2[2].

Molecular studies in SMS patients suggest a minimally deleted region (MDR) spanning approximately 700kb[3,5], though the common deletion is around 4Mb in size[4]. The proximal boundary of the MDR is within a region of overlap between the FLII and LLGL1 genes, and the distal boundary within the PEMT gene[3]. Deletions or mutations in RAI1 (Retinoic Acid Induced 1) gene, which lies within the MDR, are associated with the syndrome[3,5,6,7]. RAI1 was shown to be the primary gene responsible for most features of SMS[8,9].

Whilst deletion of the 17p11.2 region results in SMS, duplication of the same region results in a similar, yet distinct, disorder known as Potocki-Lupski syndrome[10]. Phenotypically this shares many similarities to SMS, though it is generally milder, but does have some unique clinical findings[10].

The common duplication involves the same 4Mb region as the SMS deletion as both syndromes are mediated by non-allelic homologous recombination between flanking low copy repeat regions[4].

Miller-Dieker syndrome (MDS) is a multiple malformation characterised by classical lissencephaly, a characteristic facial appearance and sometimes other birth defects[11]. It is associated with visible or submicroscopic rearrangements within chromosome band 17p13.3 in almost all cases[12]. Isolated lissencephaly sequence (ILS) consists of classical lissencephaly with no other major anomalies[13]. Submicroscopic deletions of chromosome 17p13.3 have been detected in almost 40% of these patients[12].

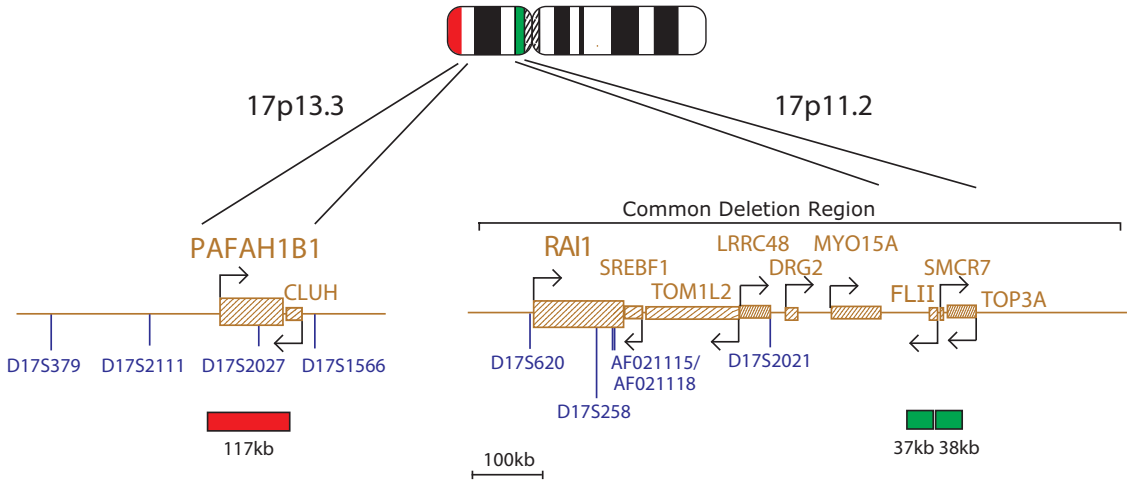
MDS is considered a contiguous gene deletion syndrome where deletion of physically contiguous genes leads to the complex phenotypic abnormalities observed. The PAFAH1B1 (LIS1) gene is located at 17p13.3 and is recognised as the causative gene for the lissencephaly phenotype in both MDS and ILS[14,15]. Deletions in MDS patients always include the PAFAH1B1 gene, together with other telomeric loci to a distance in excess of 250kb[14].

REFERENCES

1. Smith ACM et al., Am J Hum Genet 1986;24:393-414
2. Stratton RF et al., Am J Med Genet 1986;24:421-32
3. Vlangos CN et al., Am J Med Genet 2005;132A(3):278-82
4. Lupski. Nature Genetics 2007; 39:S43-S47
5. Girirajan S et al., J Med Genet 2005;42:820-8
6. Bi W et al., Am J Med Genet 2006;140(22):2454-63
7. Slager RE et al., Nat Genet 2003;33:466-8
8. Schoumans J et al., Eur J Med Genet 2005;48(3):290-300
9. Girirajan S et al., Genet Med 2006;8(7):417-27
10. Potocki et al., Am J Hum Genet 2007; 80 (4): 633–649
11. Dobyns WB et al., Am J Hum Genet 1991;48:584-94
12. Dobyns WB et al., J Am Med Assoc 1993;270:2838-42
13. Dobyns WB et al., Neurology 1992;42:1375-88
14. Chong SS et al., Hum Mol Genet 1997;6(2):147-55
15. Lo Nigro C et al., Hum Mol Genet 1997;6(2):157-64

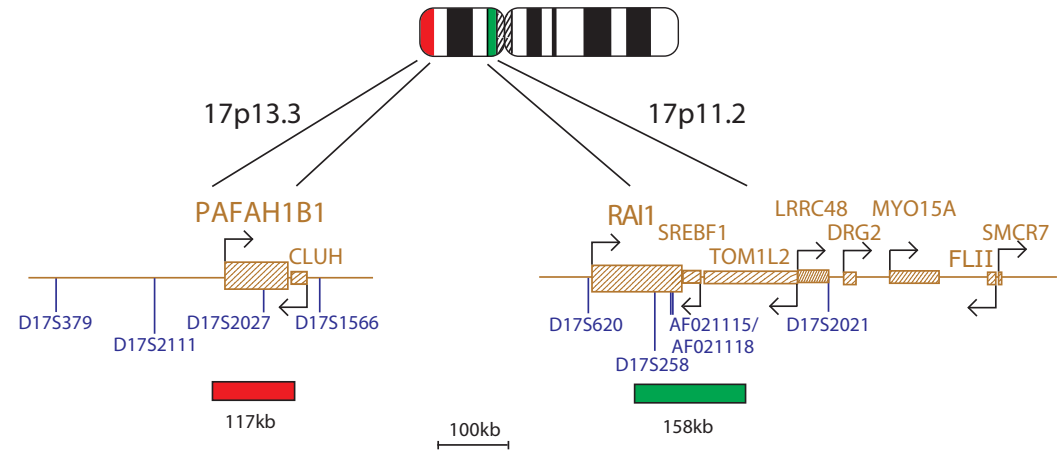
FLII

Cat. No. **LPU 007**



RAI1

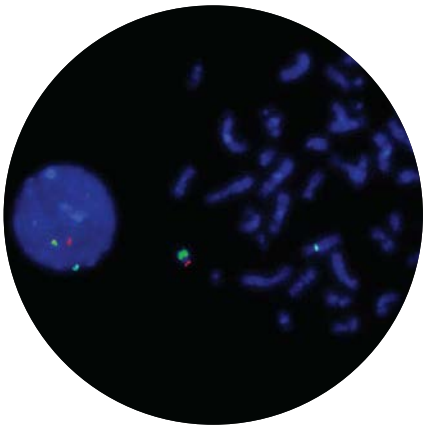
Cat. No. **LPU 019**



Cytocell an OGT company aquarius

Cat. No. **LPU 026-S** (5 tests)
Cat. No. **LPU 026** (10 tests)

SRY

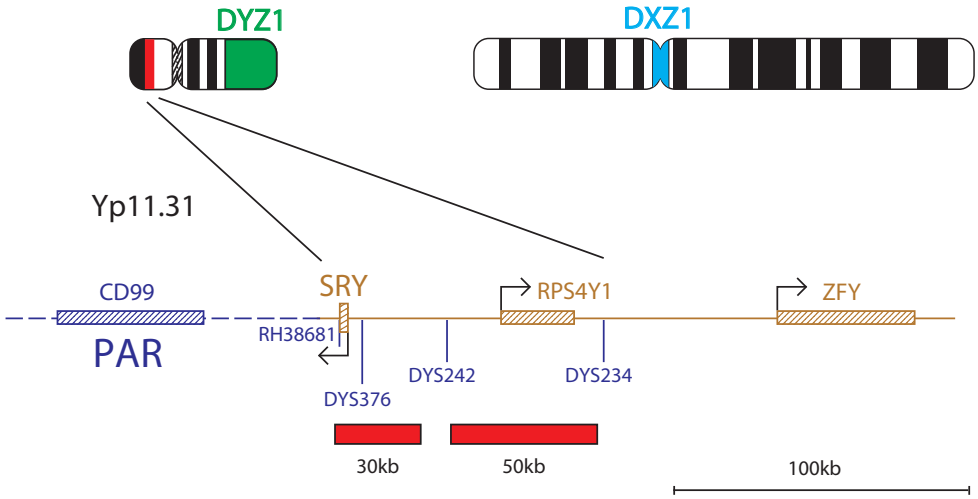


The mammalian Y-chromosomal testis-determining gene SRY (*sex-determining region Y*), located in band Yp11.31, induces male sex determination[1].

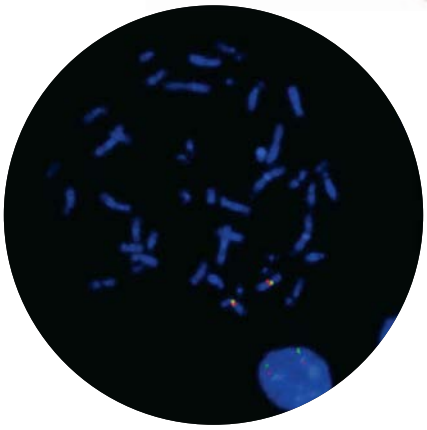
It encodes a transcription factor that is a member of the high mobility group (HMG)-box family of DNA binding proteins[2]. In mammals, it triggers the development of undifferentiated gonads into testes[3]. Human zygotes with mutations in SRY develop into XY females, while XX zygotes in the presence of SRY develop a male phenotype with occasional ambiguous genitalia[4,5]. Deletions and translocations involving the SRY region are implicated in disorders of sex differentiation[6].

REFERENCES

1. Kashimada *et al.*, Development 2010 ;137:3921-3930
2. Sinclair AH *et al.*, Nature 1990;346:240-4
3. Koopman P *et al.*, Nature 1991;351:117-21
4. Iida T *et al.*, Hum Mol Genet 1994;3:1437-8
5. Kusz K *et al.*, J Med Gene 1999;36:452-6
6. Ellaithi M *et al.*, BMC Ped 2006;6:11



Williams-Beuren

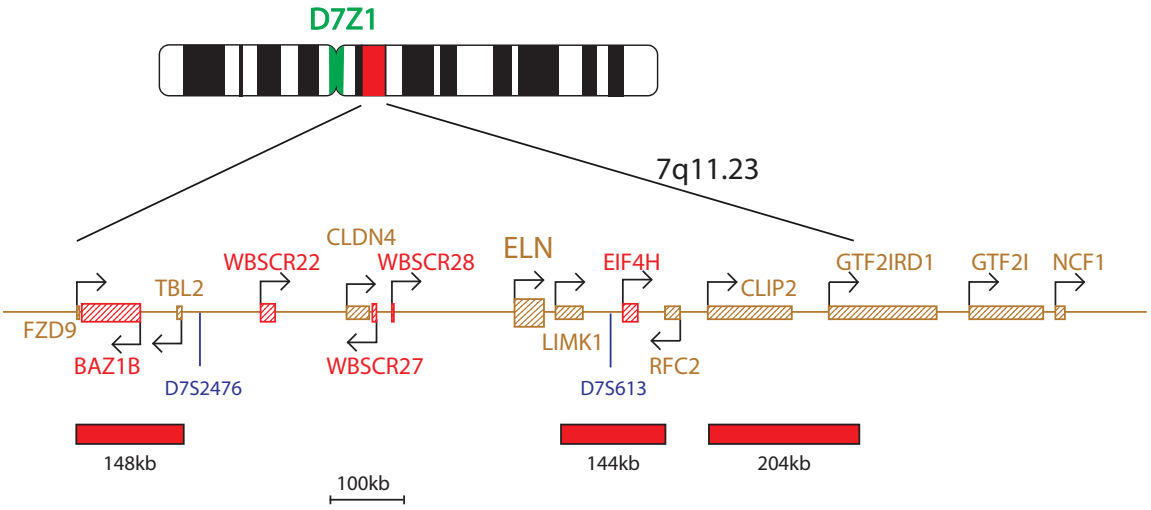


Williams-Beuren Syndrome (WBS) is a rare neurodevelopmental disorder caused by a deletion (approximately 1.5-1.8Mb in size, containing around 28 genes) within chromosome band 7q11.23[1]. The incidence of this syndrome is estimated at 1 in 7,500 to 20,000 live births[2,3,4].

Patients display a distinctive 'elfin' facial appearance, connective tissue problems, supravalvular aortic stenosis (SVAS), growth retardation, renal anomalies, transient hypercalcaemia, hyperacusis and mental retardation[5]. Haploinsufficiency of the elastin (ELN) gene has been identified as being responsible for the SVAS[6,7] but none of the other clinical features of the syndrome have been unequivocally attributed to specific genes within the WBS deleted region. These genotype-phenpotype correlations are made more difficult in WBS patients as the deletion has also been shown to have an effect on normal copy number genes that neighbour the deletion breakpoints[8].

REFERENCES

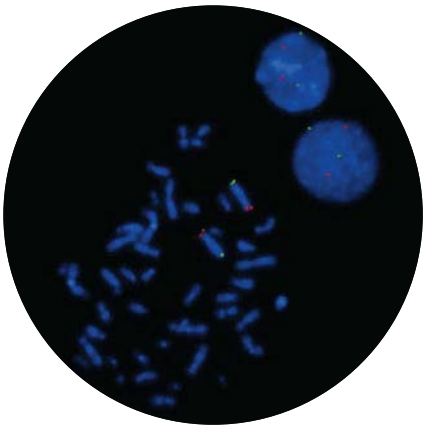
1. Francke U *et al.,* Hum Mol Genet 1999;8:1947-54
2. Stromme *et al.,* J. Child. Neurol 2002;17:269-71
3. OMIM #194050. www.omim.org/194050
4. Schubert C. Cell Mol Life Sci 2009; 66(7):1178-97
5. Pober BR, Dykens EM, Child Adolesc Psychiatr Clin North Am 1996;5:929-43
6. Ewart *et al.,* Nat Genet 1993; 5(1):11-16
7. Tassabehji M *et al.,* Hum Mol Genet 1997;6:1029-36
8. Merla *et al.,* Am J Hum Genet 2006; 79:332-341



Cytocell an OGT company aquarius

Cat. No. **LPU 009-S** (5 tests)
Cat. No. **LPU 009** (10 tests)

Wolf-Hirschhorn

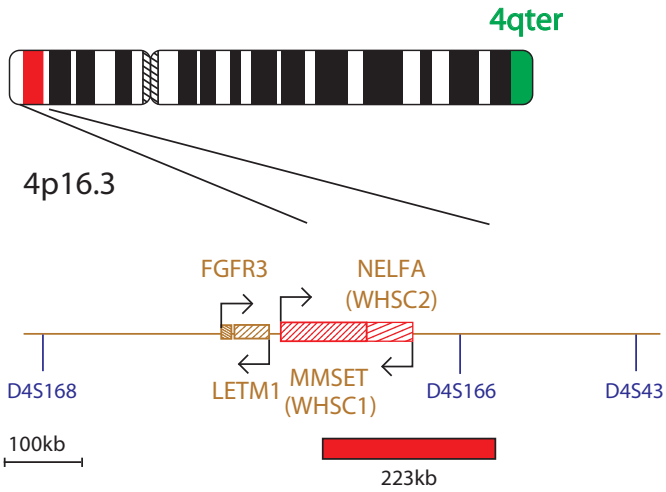


Wolf-Hirschhorn syndrome is a multiple malformation syndrome characterised by severe growth deficiency, severe to profound mental retardation with the onset of convulsions in early infancy, microcephaly, sacral dimples and a characteristic face ('Greek helmet appearance')[1,2].

The phenotype results from the partial deletion of the short arm of chromosome 4 (4p16.3). Molecular analyses of patients with small terminal and interstitial deletions have allowed the definition of the Wolf-Hirschhorn Critical Region, which is 165kb in size and lies between D4S166 and D4S3327[3].

REFERENCES

1. Wilson MG *et al.*, Hum Genet 1981;59:297-307
2. Kohlschmidt *et al.*, Prenat Diagn 2000;20(2):152-5
3. Wright TJ *et al.*, Hum Mol Genet 1997;6(2):317-24

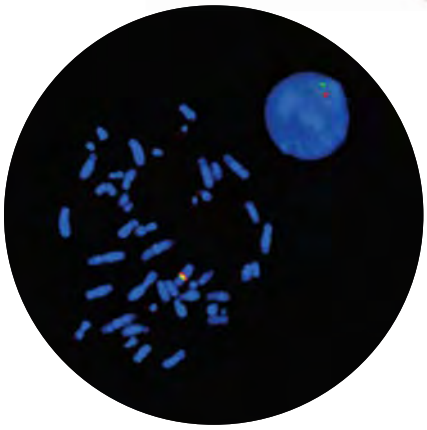


XIST

In humans, one X chromosome is inactivated in every female cell in order to achieve transcriptional balance. The X inactivation centre (XIC) is responsible for the initiation of X inactivation.

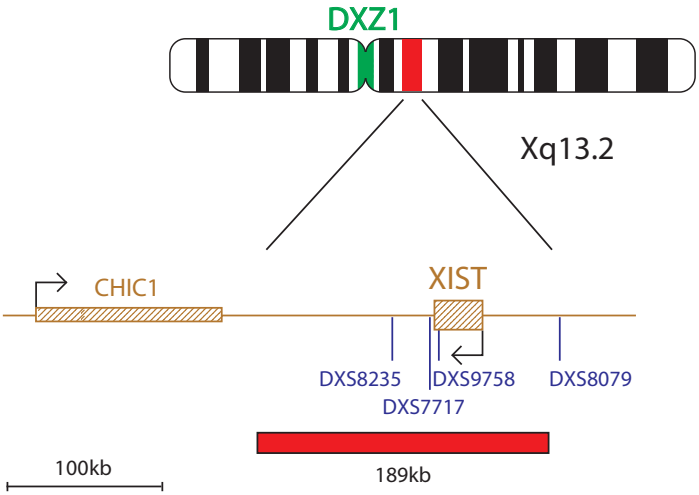
The exact size of the XIC is unclear but it includes the X-inactive specific transcript (XIST) gene at Xq13.2.This encodes a large non-coding RNA that is initially expressed on both X chromosomes before ceasing expression on the active X and becoming upregulated on the X that is to become inactivated[1]. The XIST RNA product coats the future inactive X chromosome, spreading out from the XIC.

Evaluation of marker chromosomes derived from chromosome X is important, as very small ring r(X) chromosomes that do not include the XIST gene have been associated with a more severe phenotype in syndromes such as Turner Syndrome[2,3].

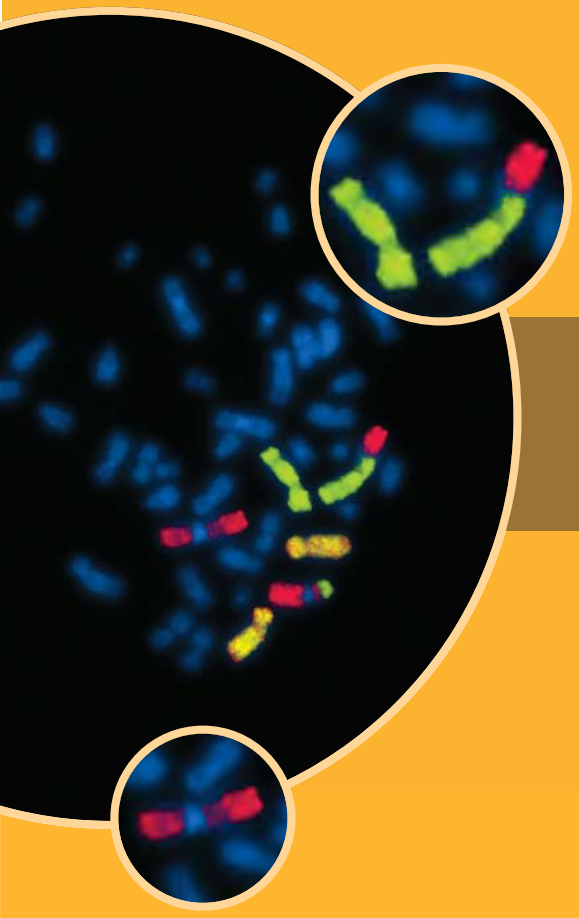


REFERENCES

1. Boumil RM, Lee JT *et al.,* Hum Mol Genet 2001;10(20):2225-32
2. Le Caignec C *et al.,* Prenat Diagn 2003;23(2):143-5
3. Bouayed Abdelmoula N, Ann Genet 2004;47(3):305-13



Cytocell
an OGT company
aquarius



Paints

Contents

Painting Probes

Cytocell's Whole Chromosome Painting Probes consist of libraries of DNA sequences derived from flow-sorted chromosomes.

These libraries contain sequences stretching over the entire length of the chromosome and provide superior coverage of each human chromosome. Applications include analysis of chromosome partners involved in translocations; identification of the chromosome of origin of marker chromosomes; confirmation of results obtained from M-FISH and SKY testing and may be of particular interest to those studying mutagenesis of human chromosomes as a result of exposure to genotoxic agents.

Cytocell offers chromosome painting probes in the Aquarius® liquid format (summarised on page 151) and on a Chromoprobe Multiprobe® device where FISH probes covering 24 chromosomes are reversibly bound to one 8 square device, illustrated on page 152.

Summary of Painting Probes

Cytocell offers a comprehensive range of Whole Chromosome Painting probes, available in the Aquarius® liquid format.

The probes are available in either a red or a green fluorophore (Texas Red® or FITC spectra respectively) and are supplied, ready-to-use, in hybridisation solution. The kits are available in an economical 5 test format and are supplied with DAPI counterstain.

Green Whole Chromosome Paints

- Cat. No. **LPP 01G**
- Cat. No. **LPP 02G**
- Cat. No. **LPP 03G**
- Cat. No. **LPP 04G**
- Cat. No. **LPP 05G**
- Cat. No. **LPP 06G**
- Cat. No. **LPP 07G**
- Cat. No. **LPP 08G**
- Cat. No. **LPP 09G**
- Cat. No. **LPP 10G**
- Cat. No. **LPP 11G**
- Cat. No. **LPP 12G**
- Cat. No. **LPP 13G**
- Cat. No. **LPP 14G**
- Cat. No. **LPP 15G**
- Cat. No. **LPP 16G**
- Cat. No. **LPP 17G**
- Cat. No. **LPP 18G**
- Cat. No. **LPP 19G**
- Cat. No. **LPP 20G**
- Cat. No. **LPP 21G**
- Cat. No. **LPP 22G**
- Cat. No. **LPP 0XG**
- Cat. No. **LPP 0YG**

Red Whole Chromosome Paints

- Cat. No. **LPP 01R**
- Cat. No. **LPP 02R**
- Cat. No. **LPP 03R**
- Cat. No. **LPP 04R**
- Cat. No. **LPP 05R**
- Cat. No. **LPP 06R**
- Cat. No. **LPP 07R**
- Cat. No. **LPP 08R**
- Cat. No. **LPP 09R**
- Cat. No. **LPP 10R**
- Cat. No. **LPP 11R**
- Cat. No. **LPP 12R**
- Cat. No. **LPP 13R**
- Cat. No. **LPP 14R**
- Cat. No. **LPP 15R**
- Cat. No. **LPP 16R**
- Cat. No. **LPP 17R**
- Cat. No. **LPP 18R**
- Cat. No. **LPP 19R**
- Cat. No. **LPP 20R**
- Cat. No. **LPP 21R**
- Cat. No. **LPP 22R**
- Cat. No. **LPP 0XR**
- Cat. No. **LPP 0YR**

Cytocell an OGT company multiprobe

Cat. No. **PMP 802** (2 devices)
Cat. No. **PMP 804** (5 devices)
Cat. No. **PMP 803** (10 devices)

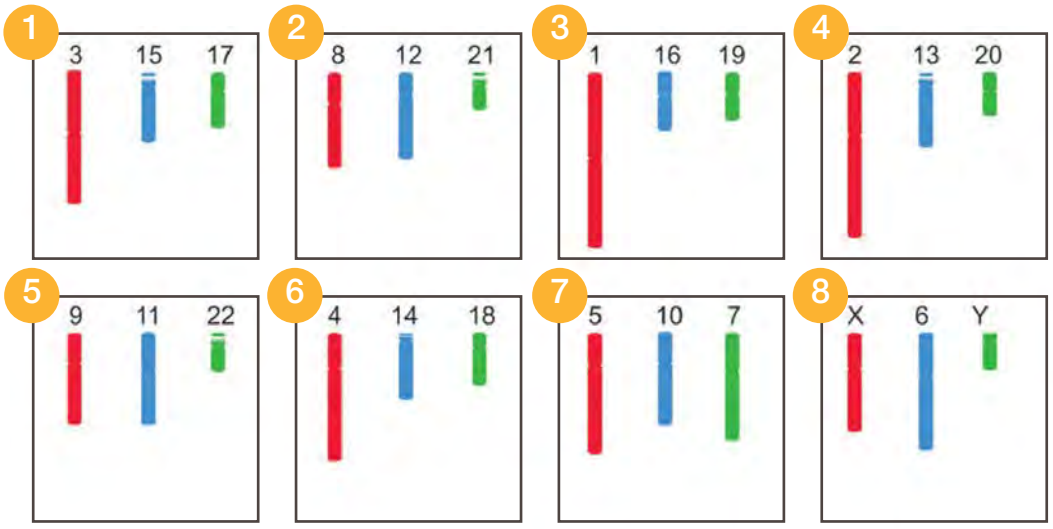
Chromoprobe Multiprobe® OctoChrome™

Cytocell's Chromoprobe Multiprobe® OctoChrome™ combines the utility of an eight square Multiprobe device and our Whole Chromosome Painting probes (labelled in three different colours), to allow all twenty-four chromosomes to be identified on a single slide.

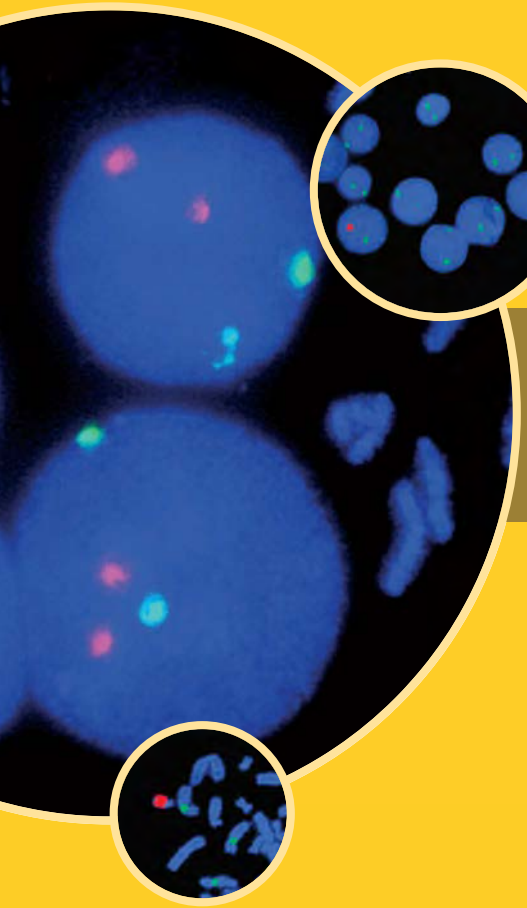
The OctoChrome™ device therefore allows simultaneous analysis of the whole genome on one slide, in one hybridisation. Each square of the device carries whole chromosome painting probes for three different chromosomes labelled in three different colour fluorophores: red, green and blue (Texas Red®, FITC and Aqua spectra, respectively). These are visible simultaneously with a DAPI/FITC/Texas Red® triple filter or individually through specific single filters.

The arrangement of chromosome combinations on the Octochrome™ device has been specifically designed to facilitate the identification of non-random chromosome rearrangements that are found in the most common leukaemias.

Chromoprobe Multiprobe® OctoChrome™ Device Layout



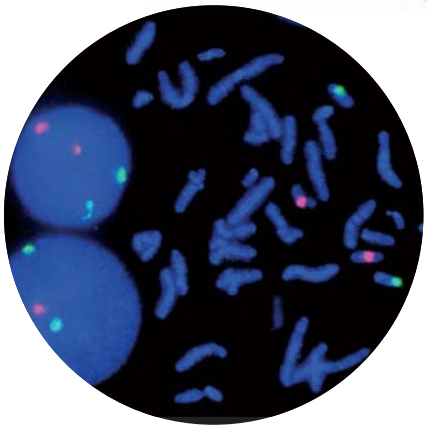
Cytocell
an OGT company
aquarius



Satellites

Contents

Satellite Enumeration Probes



Cytocell's Satellite Enumeration probes are chromosome specific sequences generated from highly repeated human satellite DNA located in the centromeric, pericentromeric or heterochromatic regions of each chromosome.

These probes allow rapid identification and enumeration of human chromosomes in interphase and metaphase cells of postnatal samples. Cytocell offers a complete range of satellite probes available in the Aquarius® liquid format. The probes are available independently and directly labelled in either red or green. They are produced in a concentrated form to allow the mixing, if required, of up to three satellite probes in the same hybridisation.

The kits are supplied in an economical 5 test format and come complete with hybridisation solution and DAPI counterstain.

Green Satellite Enumeration Probes

- Cat. No. **LPE 001G**
- Cat. No. **LPE 002G**
- Cat. No. **LPE 003G**
- Cat. No. **LPE 004G**
- Cat. No. **LPE 005G** (Chromosome 1,5,19)
- Cat. No. **LPE 006G**
- Cat. No. **LPE 007G**
- Cat. No. **LPE 008G**
- Cat. No. **LPE 009G**
- Cat. No. **LPE 010G**
- Cat. No. **LPE 011G**
- Cat. No. **LPE 012G**
- Cat. No. **LPE 013G** (Chromosome 13,21)
- Cat. No. **LPE 014G** (Chromosome 14,22)
- Cat. No. **LPE 015G**
- Cat. No. **LPE 016G**
- Cat. No. **LPE 017G**
- Cat. No. **LPE 018G**
- Cat. No. **LPE 020G**
- Cat. No. **LPE 0XG**
- Cat. No. **LPE 0YcG**
- Cat. No. **LPE 0YqG**

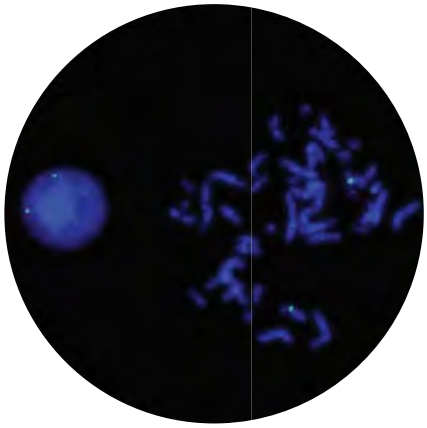
Red Satellite Enumeration Probes

- Cat. No. **LPE 001R**
- Cat. No. **LPE 002R**
- Cat. No. **LPE 003R**
- Cat. No. **LPE 004R**
- Cat. No. **LPE 005R** (Chromosome 1,5,19)
- Cat. No. **LPE 006R**
- Cat. No. **LPE 007R**
- Cat. No. **LPE 008R**
- Cat. No. **LPE 009R**
- Cat. No. **LPE 010R**
- Cat. No. **LPE 011R**
- Cat. No. **LPE 012R**
- Cat. No. **LPE 013R** (Chromosome 13,21)
- Cat. No. **LPE 014R** (Chromosome 14,22)
- Cat. No. **LPE 015R**
- Cat. No. **LPE 016R**
- Cat. No. **LPE 017R**
- Cat. No. **LPE 018R**
- Cat. No. **LPE 020R**
- Cat. No. **LPE 0XR**
- Cat. No. **LPE 0YcR**
- Cat. No. **LPE 0YqR**

Cytocell an OGT company aquarius

Cat. No. **LPE 008B** (10 tests) Cat. No. **LPE 012B** (10 tests) Cat. No. **LPE 017B** (10 tests)

Blue Labelled Satellite Enumeration Probes

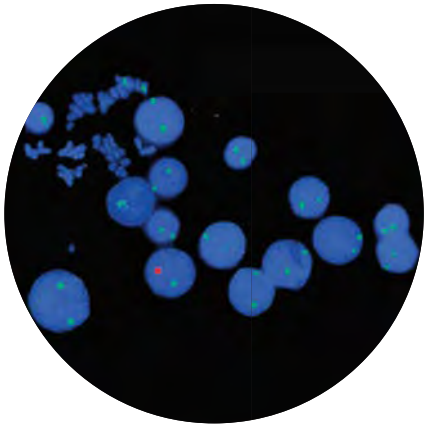


Cytocell also offers a limited range of satellite probes directly labelled in a blue fluorophore. The probes are supplied concentrated and packaged in 10 test format.

- Chromosome 8, 12, 17; other chromosomes are available through the myProbes® custom FISH probes program.

Cat. No. **LPE 0XYc** Cat. No. **LPE 0XYq**

Dual Labelled Satellite Probe Sets



XYq probe
(patient after sex-mismatched bone marrow transplant)

We also offer two dual labelled X and Y probe sets, available in the Aquarius® liquid range in a 10 test format. These may be used to identify human X and Y chromosomes in both interphase and metaphase cells.

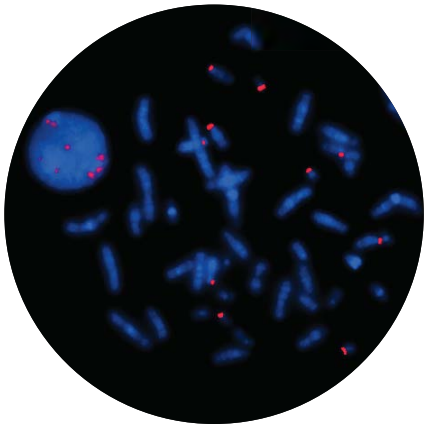
XYc: Xp11.1-q11.1 directly labelled with a green fluorophore and Yp11.1-q11.1 with a red fluorophore.

XYq: Xp11.1-q11.1 directly labelled with a green fluorophore and Yq12 with a red fluorophore.

These probes are designed for use on cultured peripheral blood and bone marrow cells.

Cat. No. **LPE NOR**

Acro-P-Arm Probe



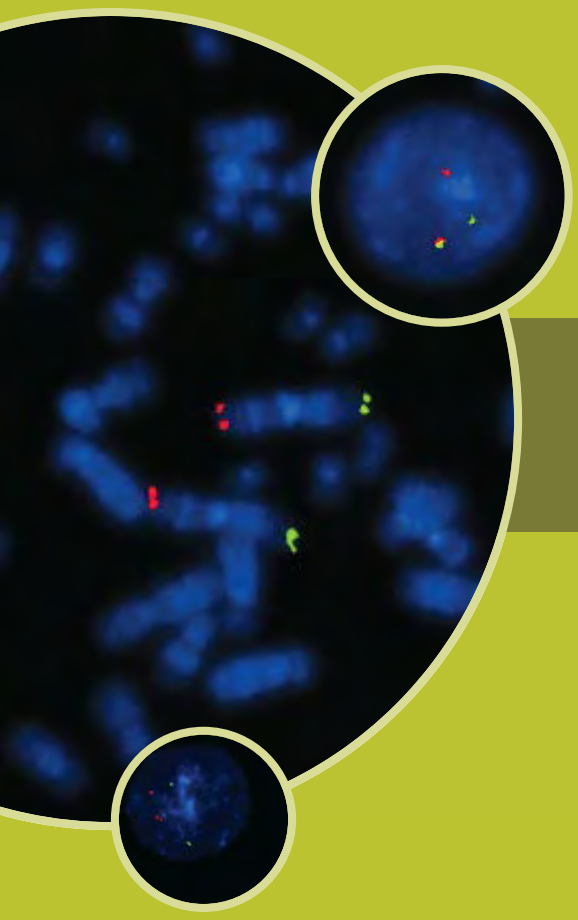
The Nucleolar Organiser Regions (NOR) contain clusters of genes which code for the three largest structural rRNA molecules (5.8S, 18S and 28S).

These rRNA genes are critically important for the viability of the cell and represent around 0.5% of the human diploid genome. They are found in the short arm of the acrocentric chromosomes and are the region around which the nucleoli develop at the end of mitosis[1]. In routine cytogenetic analysis, NOR can be used to delineate marker chromosomes through a process of silver staining the NOR (known as AgNOR staining[2]). However, the technique relies on translation of protein and if this is not present, conventional silver staining will not stain the NOR. Cytocell's FISH probe has been developed to overcome this problem so that presence of the acrocentric chromosomes in the marker can be detected.

REFERENCES

1. McClintock B, Z Zellforsch Mikrosk Anat 1934;21:294-328
2. Goodpasture C, Bloom SE, Chromosoma 1975;53:37-50

Cytocell
an OGT company



Subtelomeres

Contents

Subtelomere Specific Probes

Chromosomal rearrangements involving the ends of chromosomes have emerged as an important cause of genetic disease given the gene-rich nature of the regions adjacent to the telomeres[1]. The importance of such subtelomeric chromosome rearrangements has been clearly shown by their observed association with unexplained mental retardation and congenital abnormalities[2].

Individual subtelomere specific probes have been used to focus on particular subtelomeric regions and have resulted in the establishment of syndromes such as the chromosome 1p36 deletion syndrome[3,10] and the 22q13.3 deletion syndrome[4]. The probes are also finding applications in the investigation of autistic disorders[5], recurrent miscarriages[6] and haematological malignancies[7].

Cytocell's subtelomere specific probes are located in the most distal region of chromosome specific DNA on each chromosome. Beyond this unique sequence material is the 100 to 300kb region of telomere associated repeat followed by the cap of between 3 to 20kb of tandemly repeated (TTAGGG)n sequence[8].

The probes have been chosen from the most distal unique sequence to provide the best possible specificity, whilst also being applicable for routine use for the examination of subtelomeric enumeration and integrity.

The original second-generation set of probes is derived from PAC clones[9] and was established in conjunction with the Institute of Molecular Medicine, part of Oxford University, in the UK[11]. Continuing product improvements have led to some substitutions with alternative cosmid (35-40kb) or BAC (150kb) clones to give improved signal strength or chromosome specificity.

For references, see Chromoprobe Multiprobe®- Applications on page 163.

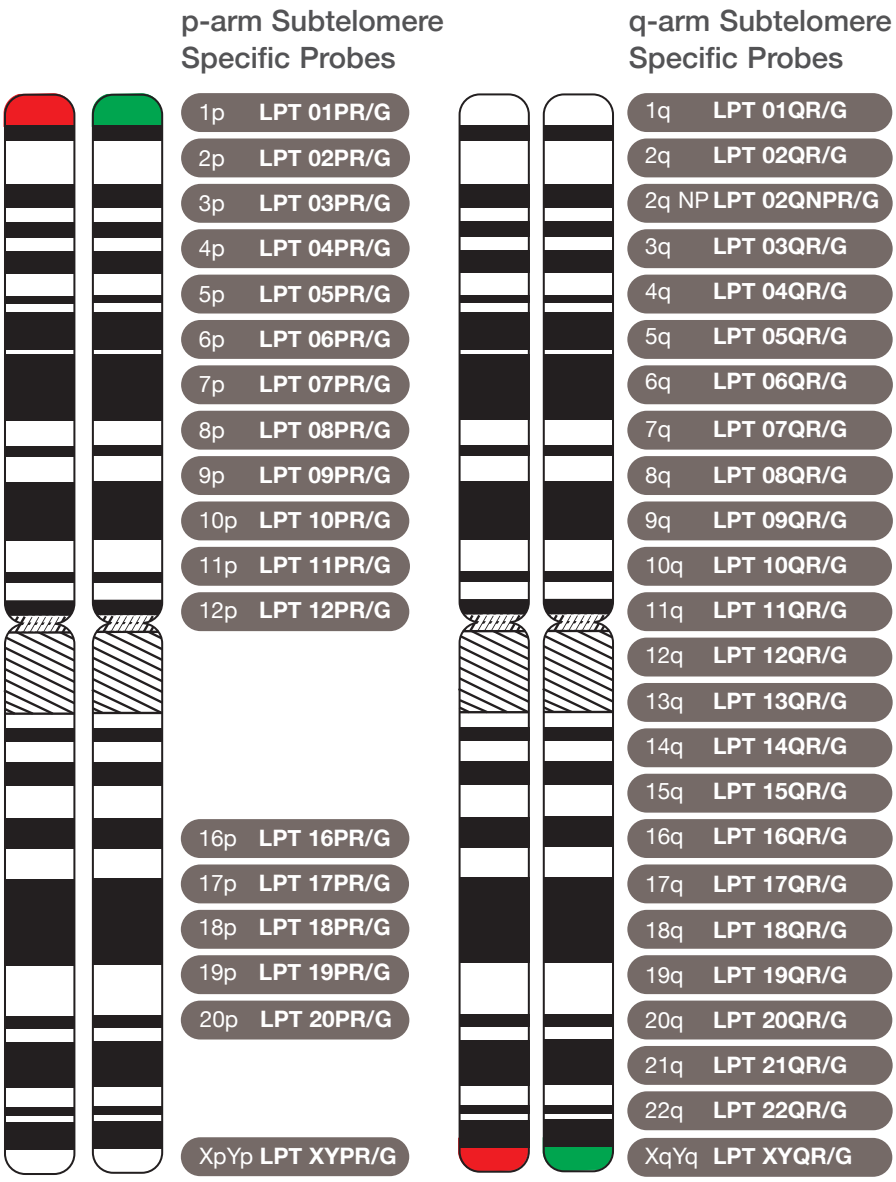
Aquarius® Subtelomere Specific Probes

Cytocell also offers a complete set of subtelomere specific probes available in the Aquarius® liquid format. The set identifies 41 of the 46 human subtelomeres with the exclusion of the p-arm telomeres of the acrocentric chromosomes.

The probes are available independently and directly labelled in either a red or a green fluorophore (Texas Red® or FITC spectra respectively).

The probes are supplied in an economical 5 test format and are concentrated to allow the mixing, if required, of up to three Aquarius® subtelomere specific probes in the same hybridisation.

The kits come complete with hybridisation solution, DAPI counterstain and full instructions for use. For probe specifications, please refer to the Aquarius® Subtelomere Specific Probe Range Summary chart in the Index section.

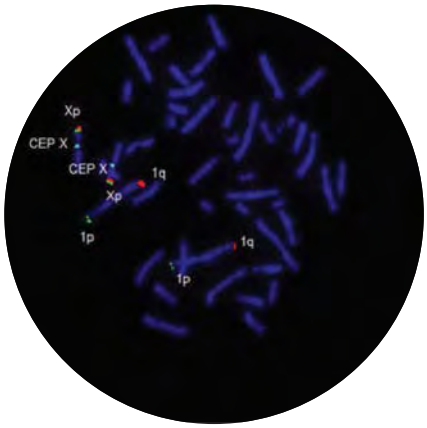


Aquarius® TeloMark Probes

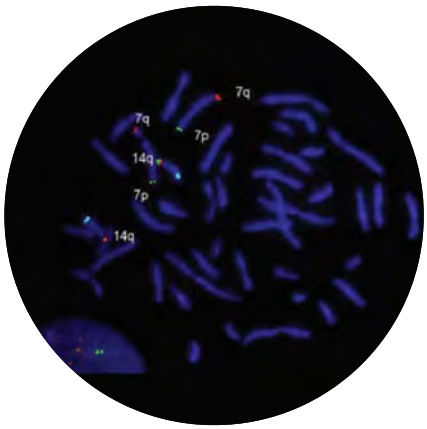
Subtelomere FISH analysis is commonly used as an adjunct to routine cytogenetic testing in order to detect small rearrangements involving the telomeric regions of chromosomes. Patients can be referred for telomere analyses for a number of different reasons, including genetic disease, autistic disorders, unexplained mental retardation/developmental delay, recurrent miscarriages and haematological malignancies[1-4].

The Cytocell TeloMark kit consists of 41 subtelomere specific probes, three centromere and six locus specific probes (50 different probes in total). The subtelomere probes represent all chromosome ends apart from the p-arms of the five acrocentric chromosomes and with no distinction between the X and Y due to clones being located in the pseudoautosomal regions. All of these probes map to unique regions of the chromosomes, within 850kb of the true telomere.

The probes in TeloMark are provided as fifteen separate mixes, either provided individually or as a kit containing all fifteen. All probes are directly labelled in orange, green, yellow (orange and green combined) or blue.



TeloMark Mix 01



TeloMark Mix 07

REFERENCES

1. De Vries *et al*., J Med Genet 2001;38:145-150
2. Knight *et al*., Am. J. Hum. Genet. 2000; 67:320-332
3. Knight *et al*., Eur. J Hum. Genet. 1997 Jan-Feb;5(1):1-8
4. Ravan *et al*., J Med Genet. 2006;43:478-489

TeloMark Product Kit

Probe Name	No. Tests	Cat. No.*
TeloMark Kit (Contains Mixes 1-15)	5 or 10	LPT MRK

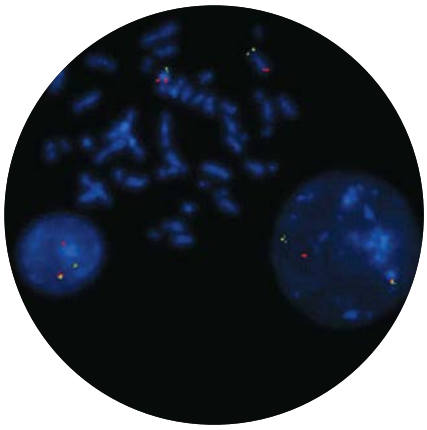
Telomark Mix	Probes	No. tests	Cat. no.*
Mix 01	1p in Green, 1q in Orange, Xp/Yp in Orange and Green (Yellow), DXZ1 in Blue	5 or 10	LPT MRK01
Mix 02	2p in Green, 2q in Orange, Xq/Yq in Orange and Green (Yellow), DXZ1 in Blue	5 or 10	LPT MRK02
Mix 03	3p in Green, 3q in Orange, 22q in Orange and Green (Yellow), BCR (22q11) in Blue	5 or 10	LPT MRK03
Mix 04	4p in Green, 4q in Orange, 21q in Orange and Green (Yellow), AML1 (RUNX1) (21q22) in Blue	5 or 10	LPT MRK04
Mix 05	5p in Green, 5q in Orange	5 or 10	LPT MRK05
Mix 06	6p in Green, 6q in Orange, 13q in Orange and Green (Yellow), 13q14 in Blue	5 or 10	LPT MRK06
Mix 07	7p in Green, 7q in Orange, 14q in Orange and Green (Yellow), TCRAD (14q11.2) in Blue	5 or 10	LPT MRK07
Mix 08	8p in Green, 8q in Orange, 17p in Orange and Green (Yellow), D17Z1 in Blue	5 or 10	LPT MRK08
Mix 09	9p in Green, 9q in Orange, 17q in Orange and Green (Yellow), D17Z1 in Blue	5 or 10	LPT MRK09
Mix 10	10p in Green, 10q in Orange, 15q in Orange and Green (Yellow), PML (15q24) in Blue	5 or 10	LPT MRK10
Mix 11	11p in Green, 11q in Orange, 18p in Orange and Green (Yellow), D18Z1 in Blue	5 or 10	LPT MRK11
Mix 12	12p in Green, 12q in Orange, 18q in Orange and Green (Yellow), D18Z1 in Blue	5 or 10	LPT MRK12
Mix 13	16p in Green, 16q in Orange	5 or 10	LPT MRK13
Mix 14	19p in Green, 19q in Orange, E2A (TCF3) (19p13) in Blue	5 or 10	LPT MRK14
Mix 15	20p in Green, 20q in Orange	5 or 10	LPT MRK15

*for 5 test kit, add -S to catalogue number, e.g: LPT MRK##-S

Cytocell an OGT company multiprobe

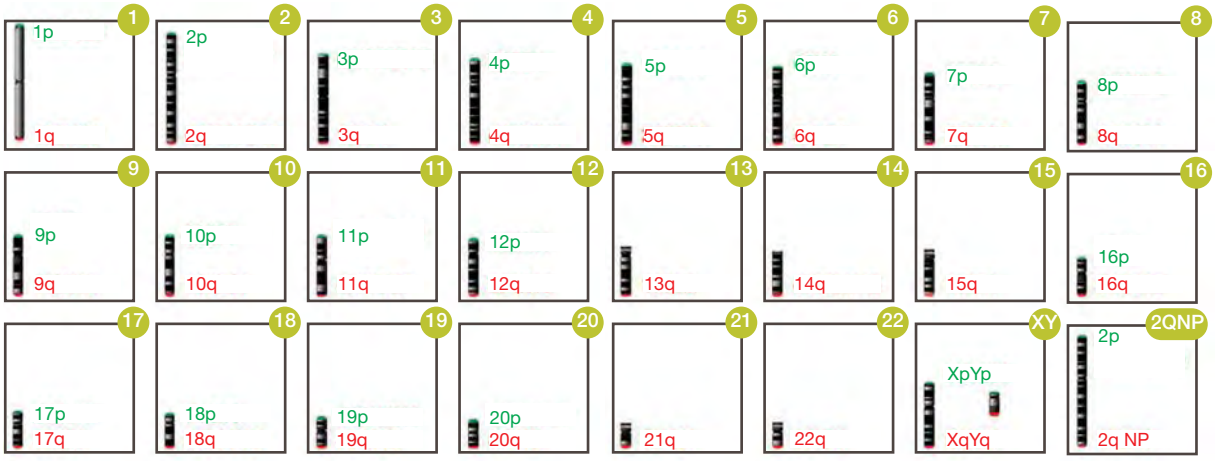
Cat. No. **PMP 009** (2 devices)
Cat. No. **PMP 008** (5 devices)
Cat. No. **PMP 007** (10 devices)

Chromoprobe Multiprobe® -T System

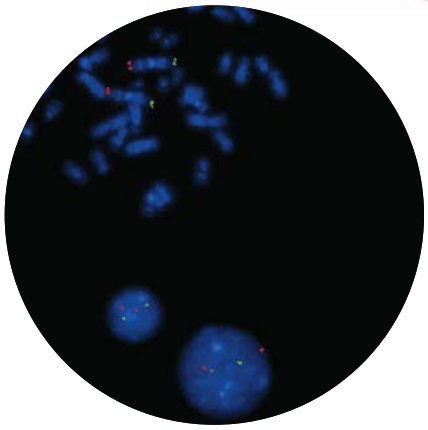


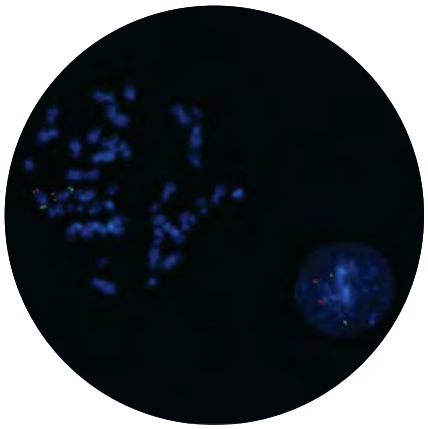
The Chromoprobe Multiprobe®-T system is divided into 24 squares. Each square carries subtelomere specific probes for both the p-arm and the q-arm of one of the 23 chromosomes (except for the acrocentric chromosomes).

The p-arm and the q-arm probes for each chromosome are labelled in different colours with two spectrally independent fluorophores (green and red respectively). These are located together in the corresponding Multiprobe square. This format provides each other with an internal hybridisation control and effective chromosome identification.



Chromoprobe Multiprobe® -T System Applications





Subtelomeric rearrangements in idiopathic mental retardation and/or in malformation syndromes

Over the past 20 years, there have been numerous large and small scale studies that have shown the importance of subtelomeric chromosome rearrangements as a major cause of mental retardation and/or malformation syndromes. The largest study, involving screening of 11,688 cases, reported clinically significant subtelomeric abnormalities in around 2.5% of cases, with an additional 0.5% detection rate of familial variants[12]. Previous studies showed abnormality rates to be between 2 and 29%, with the large variance in figures most likely being due to sampling biases, with estimates being higher in patients with moderate to severe metal retardation than those with a mild version[12,13,14].

The Chromoprobe Multiprobe®-T System assay allows, in one single experiment, the identification of subtle chromosome rearrangements in patients suspected of carrying a chromosome anomaly, but who have an apparently normal karyotype.

Characterisation of known abnormalities

Subtelomeric chromosome rearrangement screening has been clearly associated with the establishment of new syndromes such as the chromosome 1p36 deletion syndrome[10] and the 22q13.3 deletion syndrome[11].

Autistic disorders

Several reports have associated subtelomeric chromosomal rearrangements with autistic disorders[5].

Recurrent miscarriages

Subtelomeric rearrangements are also being investigated in recurrent miscarriages[6].

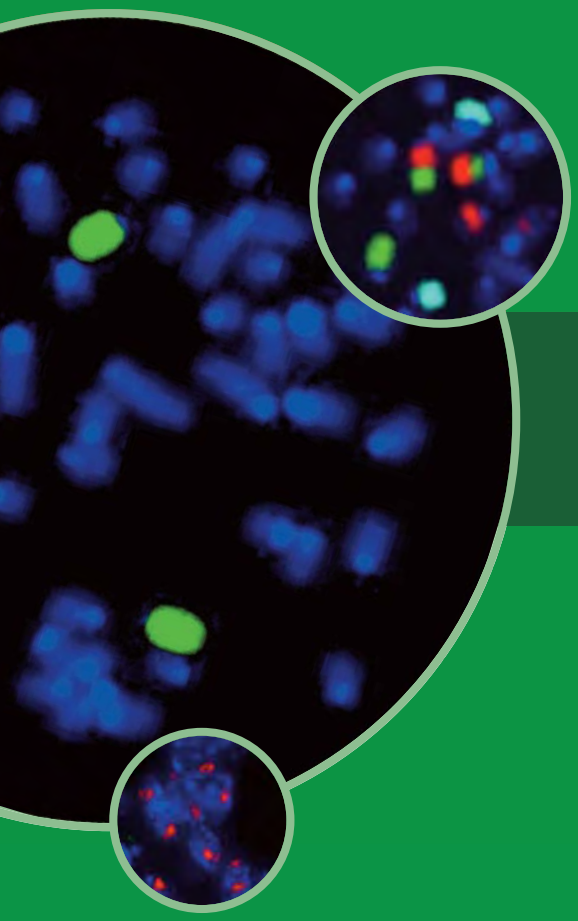
Haematological cancers

Other clinical applications include the characterisation of haematological abnormalities[7] initially detected by standard cytogenetic studies but where further submicroscopic rearrangements cannot be ruled out by the limited resolution of standard karyotyping. Therefore, telomere screening provides confirmation and further characterisation of these cases.

REFERENCES

1. Saccone *et al.,* Proc Natl Acad Sci USA 1992;89(11):4913-7
2. Flint *et al.,* Nat Genet 1997;15(3):252-7
3. Heilstedt *et al.,* Clin Genet 2003;64(4):310-6
4. Luciani *et al.,* J Med Genet 2003;40(9):690-6
5. Wolff *et al.,* Genet in Med 2002;4(1):10-4
6. Yakut *et al.,* Clin Genet 2002;61(1):26-31
7. Tosi *et al.,* Genes Chrom Cancer 1999;25(4):384-92
8. Moyzis *et al.,* Proc Natl Acad Sci USA 1988;85:6622-6
9. Knight *et al.,* Am J Hum Genet 2000;67:320–32
10. Institute of Molecular Medicine and National Institute of Health Collaboration, Nat Genet 1997;14:86-9
11. Knight *et al.,* Eur J Hum Genet 1997;5:1-6
12. Ravnan *et al.,* J Med Genet 2006;43:478–489
13. Biesecker LG. Am J Med Genet 2002;107:263–6
14. Knight *et al.,* Lancet 1999;354(9191):1676–81

Cytocell
an OGT company
aquarius



ZooFISH

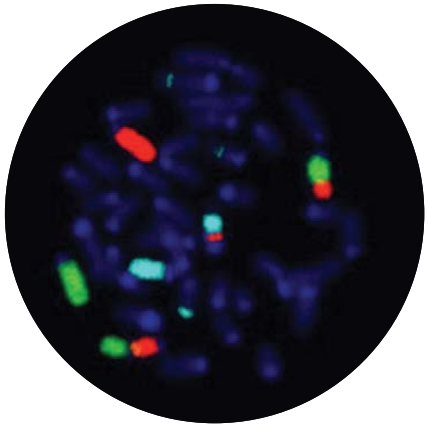
ZooFISH

For information regarding products soon to be available in the Cytocell ZooFISH probe range, or to discuss your requirements for a custom ZooFISH probe, please email contact@ogt.com

ZooFISH Range

Chromoprobe Multiprobe OctoChrome Murine*

The Cytocell Chromoprobe Multiprobe OctoChrome Murine (OctoChrome Murine) is designed to identify aneuploidies and translocations present in the entire mouse karyotype. The system utilises mouse whole chromosome painting (WCP) probes directly labelled in three different colours, which allows the visualisation of chromosomal abnormalities under the fluorescence microscope without expert knowledge of the mouse karyotype.



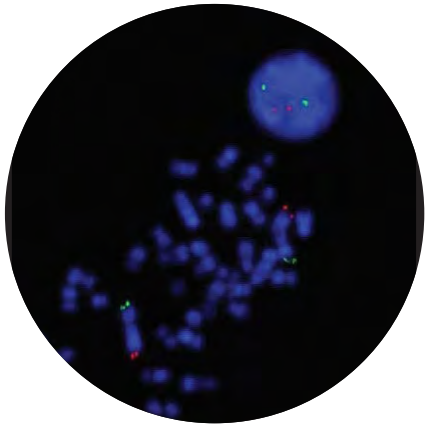
Chromoprobe Multiprobe OctoChrome Murine

	1,4,14	2,5,15	3,7,16	6,8,17
	10,9,18	12,11,19	X,13,Y	

Figure 1: The OctoChrome Murine device layout. Each square of the OctoChrome Murine device carries mouse whole chromosome painting probes for three different chromosomes labelled in red, green and aqua blue (Texas Red®, FITC and aqua spectra, respectively); these probes are reversibly dried on to the first 7 squares of the device using a proprietary process. FISH signals are visible simultaneously with a DAPI/FITC/Texas Red® triple filter or individually through specific single fluorescence filters.

Chromoprobe Multiprobe Porcine*

The Cytocell Chromoprobe Multiprobe Porcine is a useful tool in the pig breeding industry to identify translocations that have implications in fertility. The system allows the user to perform multiple FISH experiments on a single slide and to detect chromosomal aberrations (aneuploidy, chromosome breakage and rearrangements) present in the pig karyotype. The Chromoprobe Multiprobe Porcine utilises directly-labelled locus-specific subtelomere BAC probes, allowing the visualisation of any chromosomal aberrations under the fluorescence microscope without expert knowledge of the pig karyotype.



Chromoprobe Multiprobe Porcine

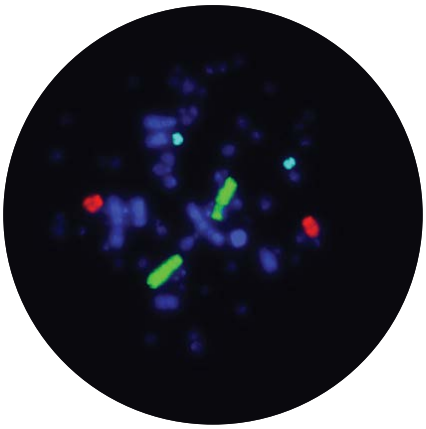
*For research use only, not for use in diagnostic procedures.

	1pq	2pq	3pq	4pq	5pq	6pq	7pq	8pq
	9pq	10pq	11pq	12pq	13pq	14pq	15pq	16pq
	17pq	18pq	Xpq					

Figure 2: The Chromoprobe Multiprobe Porcine device layout. Each square of the device carries two subtelomeric BAC probes labelled in red and green fluorochromes (Texas Red®, FITC). The probes are reversibly dried on to the first 19 squares of the device using a proprietary process. FISH signals are visible with a DAPI/FITC/Texas Red® triple filter or individually through specific single filters.

Chromoprobe Multiprobe Chicken*

The chicken genome consists of a large number of microchromosomes; therefore, analysis of the chicken genome by classical cytogenetics is extremely complex. The Cytocell Chromoprobe Multiprobe Chicken is designed to identify complex chromosome rearrangements present in the chicken karyotype (1-28, Z and W). The system utilises directly-labelled whole chromosome painting (WCP) probes and locus-specific subtelomere BAC probes that allow the visualisation of chromosomal rearrangements under the fluorescent microscope without expert knowledge of the chicken karyotype.



Chromoprobe Multiprobe Chicken

	10pq	11pq	12pq	13pq	14pq	15pq	16pq	17pq
	1,4,3	18pq	2,5,8	19pq	6,7,9	20pq	Z,W	21pq
	22pq	23pq	24pq	25pq	26pq	27pq	28pq	

Figure 3: The Chromoprobe Multiprobe Chicken device layout. Each square of the devices carries either chicken chromosome paints for three different chromosomes (macro) labelled in red, green and aqua (Texas Red®, FITC and aqua spectra, respectively); or subtelomeric BAC probes labelled in red and green fluorochromes (Texas Red®, FITC). The probes are reversibly dried on to the first 23 squares of the device using a proprietary process. FISH signals are visible with a DAPI/FITC/Texas Red® triple filter or individually through specific single fluorescence filters.

*For research use only, not for use in diagnostic procedures.

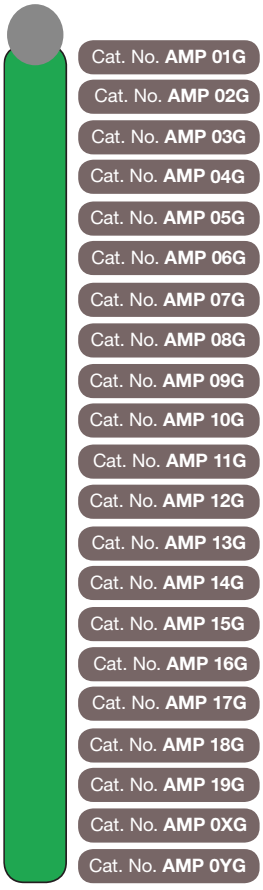
Murine Painting Probes*

Cytocell offers a comprehensive range of Murine Whole Chromosome Painting probes for the assessment of chromosome number, breakage or rearrangement. Our Whole Chromosome Paints were initially developed from flow sorted *Mus musculus* chromosomes in the laboratory of Prof. Malcolm Ferguson-Smith, Cambridge University Department of Veterinary Medicine, UK.

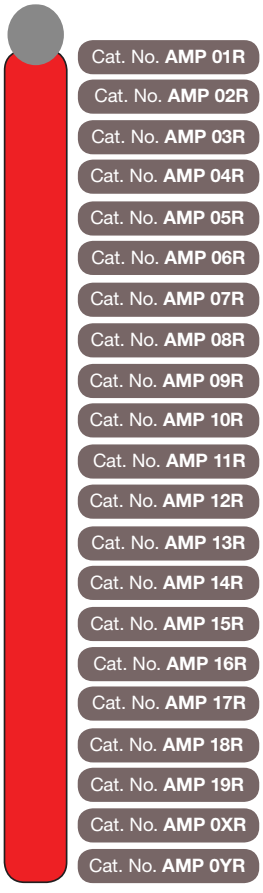
With current advances in murine research, Cytocell has optimised each of the Murine Painting probes for use on formalin-fixed paraffin embedded (FFPE) tissue and fixed cell suspensions. Having reviewed current laboratory practices, we are the only manufacturer to offer optional hybridisation times – 4 hours or overnight. The probes are available in either a red or a green fluorophore (Texas Red® or FITC spectra respectively) to enable multiple paints to be combined in a single reaction. They are provided ready-to-use in hybridisation solution and supplied with DAPI counterstain. The kits are available in an economical 50 l or 100 l format.

Aquarius® Murine Whole Chromosome Painting probes provide you with the advantage of:

- ***FAST*** **hyb. time – 4 hours or overnight**
- **Ability to mix multiple paints**
- **Simple FISH protocol**
- **Minimal background**
- **Multiple sample types**
- **Ready-to-use reagents**
- **Specific high intensity signals**
- **Economical kit format**



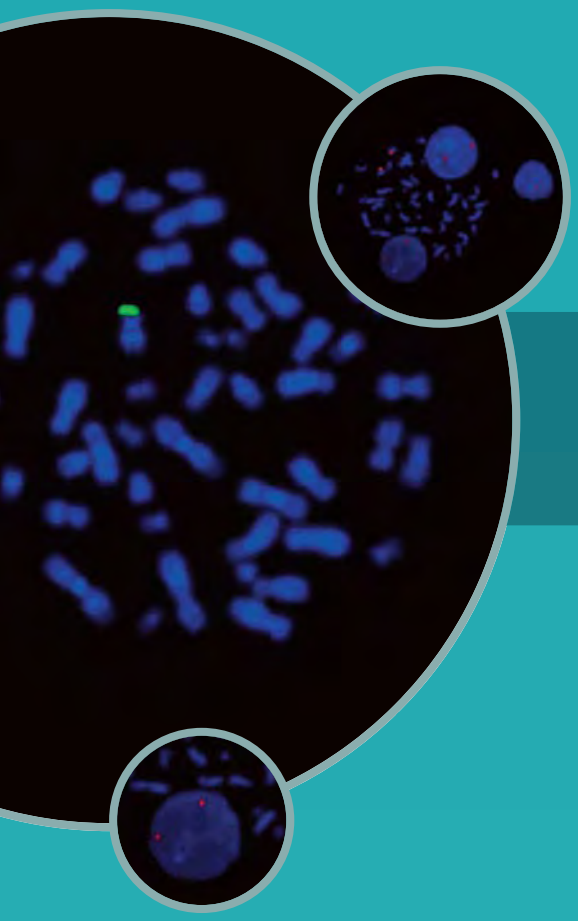
Cat. No. **AMP 01G**
Cat. No. **AMP 02G**
Cat. No. **AMP 03G**
Cat. No. **AMP 04G**
Cat. No. **AMP 05G**
Cat. No. **AMP 06G**
Cat. No. **AMP 07G**
Cat. No. **AMP 08G**
Cat. No. **AMP 09G**
Cat. No. **AMP 10G**
Cat. No. **AMP 11G**
Cat. No. **AMP 12G**
Cat. No. **AMP 13G**
Cat. No. **AMP 14G**
Cat. No. **AMP 15G**
Cat. No. **AMP 16G**
Cat. No. **AMP 17G**
Cat. No. **AMP 18G**
Cat. No. **AMP 19G**
Cat. No. **AMP 0XG**
Cat. No. **AMP 0YG**



Cat. No. **AMP 01R**
Cat. No. **AMP 02R**
Cat. No. **AMP 03R**
Cat. No. **AMP 04R**
Cat. No. **AMP 05R**
Cat. No. **AMP 06R**
Cat. No. **AMP 07R**
Cat. No. **AMP 08R**
Cat. No. **AMP 09R**
Cat. No. **AMP 10R**
Cat. No. **AMP 11R**
Cat. No. **AMP 12R**
Cat. No. **AMP 13R**
Cat. No. **AMP 14R**
Cat. No. **AMP 15R**
Cat. No. **AMP 16R**
Cat. No. **AMP 17R**
Cat. No. **AMP 18R**
Cat. No. **AMP 19R**
Cat. No. **AMP 0XR**
Cat. No. **AMP 0YR**

*For research use only, not for use in diagnostic procedures.

myProbes
POWERED BY Cytocell
an OGT company



Custom FISH Probes

myProbes
POWERED BY Cytocell
an OGT company

myProbes® Custom FISH Probes*

Custom FISH Probes designed to your specifications

myProbes custom probes are:

- Fully quality-assured
- Manufactured under GMP & GLP guidelines
- Made under a quality system certified to ISO13485:2003 and ISO9001:2008 quality standards

myProbes is a custom design and manufacture service that provides unique fluorescence *in situ* hybridisation (FISH) probes using the BAC-2-FISH™ process. This process utilises Cytocell's proprietary BAC clone collection containing >220,000 clones to produce fully quality-assured custom FISH probes for virtually any sequence in the entire human genome.

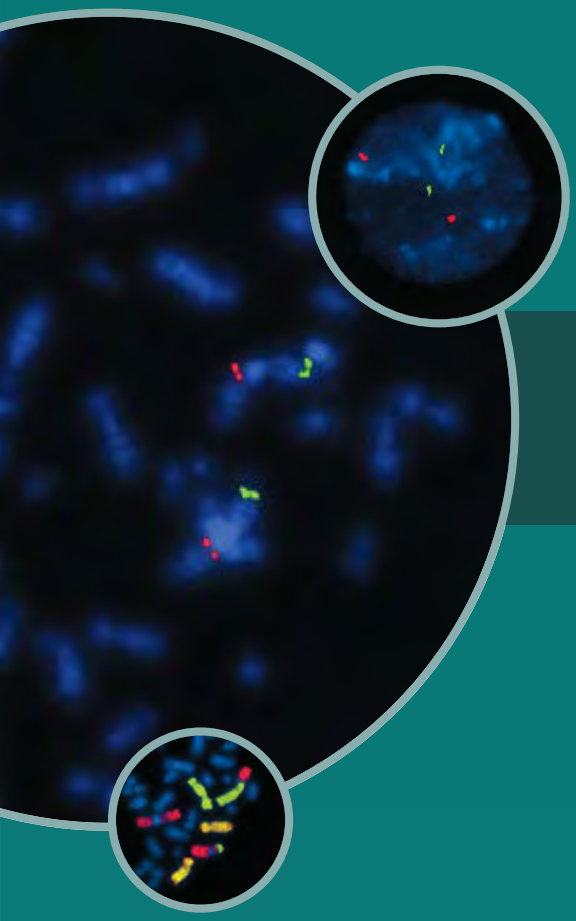
Based on your specific interests and research, custom FISH probes may range from a simple catalogue probe modification to a truly unique product.

All custom myProbes are tested on your specific sample type (when available) to ensure reproducibility. Our process and quality assurances are designed to produce high-quality probes and accurate results.

To learn more about the myProbes process, email contact@ogt.com

*For research use only, not for use in diagnostic procedures.

Cytocell
an OGT company
aquarius



FISH Accessories

Cytocell
an OGT company

Accessories

Accessories

Cat. No.	Description	Unit Size
PCN004	Hybridisation Chamber	1
PCN007	24 Square Template Slides	100
PCN008	8 Square Template Slides	100
PCN002	Cytocell Slide Surface Thermometer	4

Ancillary Reagents

Cat. No.	Description	Unit Size
PCA005	Rubber Solution Glue	15g
PCN003	Mounting Medium	10ml
DES500L	0.125µg/ml DAPI	500µl
DES1000L	0.125µg/ml DAPI	1000µl
DFS500L	1.0µg/ml DAPI	500µl
DSS500L	0.0625µg/ml DAPI	500µl
HA500L	Hybridisation Solution A	500µl
HA1000L	Hybridisation Solution A	1000µl
HB500L	Hybridisation Solution B	500µl
HB1000L	Hybridisation Solution B	1000µl
PCA003	20x SSC	100ml

Microscope Filters*

Cat. No.	Description	Unit Size
N/A	FITC Filter	1
N/A	DAPI Filter	1
N/A	Texas Red Filter®	1
N/A	DEAC Filter	1
N/A	FITC/Texas Red® Dual Filter	1
N/A	FITC/DAPI/Texas Red® Triple Filter	1

* Filter cubes are available upon request, please specify the name of the microscope manufacturer and model name/number.

SureSeq™

Next Generation Sequencing (NGS)

Contents

SureSeq™

Overview

The application of next generation sequencing (NGS) technologies to cancer research in recent years has provided novel insights into disease initiation, progression and response to therapy. This powerful technique allows for accurate analysis of nucleotide-level aberrations such as single nucleotide variants (SNVs) and small insertions and deletions (indels).

SureSeq™ NGS products include targeted sequencing panels for the accurate detection of genetic variants and library preparation products for a streamlined NGS workflow.

Utilising hybridisation-based enrichment, SureSeq NGS cancer panels deliver excellent uniformity of coverage, greater run-to-run consistency and ensure highly reproducible data. These factors are particularly important when studying heterogeneous cancer samples, where the ability to detect mutations with low minor allele fractions (MAF) at high accuracy is required. In addition, hybridisation-based enrichment allows for detection and removal of PCR bias, which is not possible when using amplicon-based assays.

SureSeq panels are designed with the most up-to-date content and to meet the throughput needs, cost considerations and quality standards of leading research laboratories. Customisation of panels is also possible, please enquire.

SureSeq™

Cat. No. **600073** (16 reactions)
Cat. No. **600074** (96 reactions)

SureSeq Ovarian Cancer Panel

Hybridisation-based NGS panel validated on FFPE samples and whole blood; it allows the analysis of variants associated with ovarian cancer and research into therapeutic response

The SureSeq Ovarian Cancer Panel:

- Contains the latest evidence-based genes involved in ovarian cancer research — gain insight into homologous repair deficiencies and cell cycle dysregulation
- Validated for research use on FFPE and whole blood — detect germline mutations in DNA derived from blood as well as both germline and somatic mutations in DNA derived from FFPE tissue
- Utilises hybridisation-based enrichment — sensitive and reproducible detection of low-frequency variants, even in heterogeneous cancer samples
- Fast and easy workflow — streamlined library preparation, short 4-hour hybridisation and intuitive software allowing easy variant analysis
- Delivers excellent uniformity of coverage across the whole panel — over 99% of targeted regions are covered to at least 20% of mean target coverage

Ovarian cancer is the leading cause of death from gynaecological cancers in the Western world[1]. Next generation sequencing (NGS) is quickly becoming a commonly used tool for analysis of mutations — both single nucleotide variants (SNVs) and insertion/deletions (indels) — in genes associated with ovarian cancer. The SureSeq Ovarian Cancer Panel has been developed with leading cancer experts and covers all coding exons of seven genes (Table 1). The panel allows detection of known and novel variants in tumour suppressor genes as well as genes involved in homologous repair to advance research into ovarian cancer treatment. It has been validated on DNA derived from FFPE tissue and whole blood to allow investigation of both germline and somatic mutations.

Utilising hybridisation-based enrichment, the SureSeq Ovarian Cancer Panel delivers excellent run-to-run consistency and extremely uniform coverage across the whole region of interest (Figure 1) to allow sensitive detection of variants present, even at low minor allele fraction (MAF) (Table 2).

The SureSeq Ovarian Cancer panel is optimised to work with the SureSeq NGS Library Preparation Kit. For more information, see page 184.

REFERENCES

1. Helleman J. *et al.* (2006) Molecular profiling of platinum resistant ovarian cancer. Int J Cancer 118(8):1963-71

BRCA1	BRCA2	TP53	PTEN	ATM	ATR	NF1

Table 1: The SureSeq Ovarian Cancer Panel targets seven genes implicated in ovarian cancer.

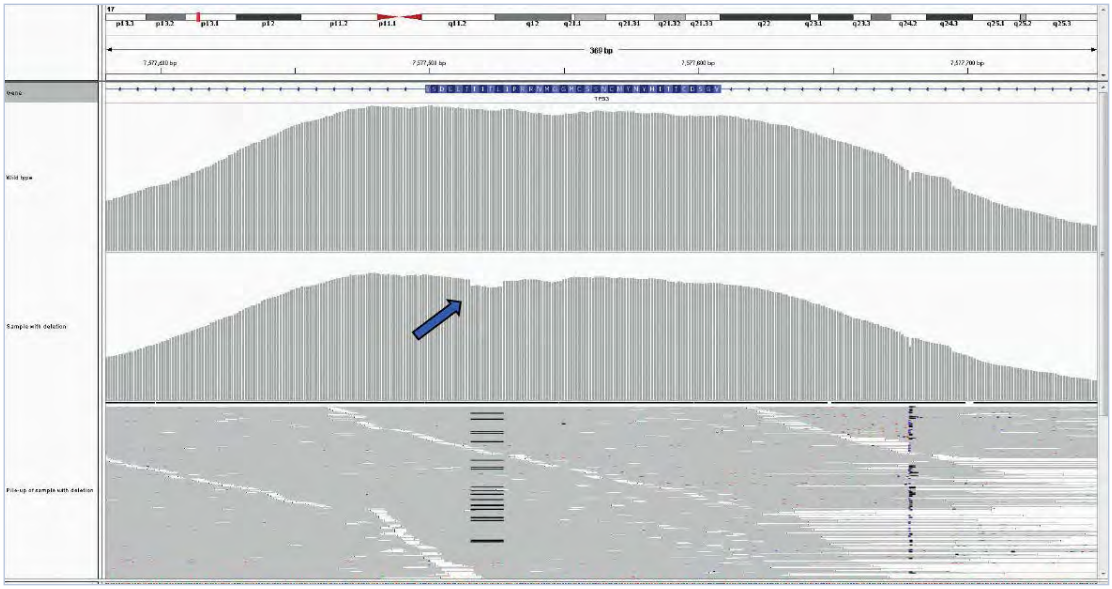


Figure 1: OGT's expert bait design delivers excellent uniformity of coverage. Shown here is FFPE sample, exon 7 of *TP53* (NM_000546). The top panel shows a normal control, the bottom panel shows a deletion (c.754_765delCTCACCATCATC) at 6% frequency. Mean target coverage >1400x, 12 samples per MiSeq lane.

Gene	Variant detected	Type of variant	Mean target coverage	% MAF detected
BRCA1	c.3424G>C (p.Ala1142Pro)	SNV	881	11.92%
BRCA2	c.556G>C (p.Ala186Pro)	SNV	728	1.92%
TP53	c.1129A>C (p.Thr377Pro)	SNV	1024	3.03%
ATR	c.7274G>A (p.Arg2425Gln)	SNV	1579	38.63%
NF1	c.8137_8138insG (p.Phe2714ValfsTer16)	Insertion	683	1.45%
NF1	c.3354delT (p.Ser1118ArgfsTer24)	Deletion	621	1.13%
ATR	c. 4154delC (p.Thr1385MetfsTer3)	Deletion	506	1.61%

Table 2: Example mutations detected in FFPE clinical research samples using the SureSeq Ovarian Cancer Panel. The ability to detect MAFs as low as 1.13% gives added confidence in the variants being called and facilitates the exploration of tumour heterogeneity. Rows 1–4: low-frequency SNVs; rows 5–7: low-frequency indels. Samples kindly provided by Biopathology Department of Gustave Roussy, Villejuif, France.

SureSeq™

Cat. No. **600075** (16 reactions)
Cat. No. **600076** (96 reactions)

SureSeq Myeloid Panel

25-gene myeloid disorders hybridisation-based NGS enrichment panel that delivers accurate and easy identification of variants

The SureSeq Myeloid Panel delivers:

- Most up-to-date content designed in collaboration with recognised cancer experts — detect SNVs and indels in 25 genes implicated in a variety of MPNs
- Time and cost saving solution — replace multiple single gene assays with one comprehensive panel
- Sensitive and reproducible variant detection even in heterogeneous samples — detect low-frequency alleles down to 1% MAF with confidence
- Fast and easy workflow — streamlined library preparation, rapid hybridisation and intuitive software allowing easy variant analysis
- Excellent coverage uniformity — 99% of targeted regions are covered to at least 20% of mean target coverage

Myeloproliferative neoplasms (MPNs) are a group of diseases that affect normal blood cell production in the bone marrow resulting in overproduction of one or more cell types (i.e. red cells, white cells or platelets). There are numerous different sub-types of MPNs that are distinguished from each other by the type of cell which is most affected and the genetic profile. The SureSeq Myeloid Panel targets selected key genes known to contain driver mutations for a range of MPNs including polycythaemia vera (PV), essential thrombocythaemia (ET) and myelofibrosis (MF) (Table 1). To obtain the optimal sensitivity whilst maximising throughput, hot exons where clinically relevant mutations are known, and every exon for tumour suppressor, hereditary and highly implicated research-related genes, are targeted. This allows detection of previously characterised as well as novel variants in myeloid samples.

Instead of assaying for single genes in a sequential manner, the mutational status of 25 genes can be rapidly and simultaneously determined with the use of the SureSeq Myeloid Panel.

The SureSeq Myeloid Panel has been validated with samples from the National Institute for Biological Standards and Control (NIBSC) and has been shown to accurately detect alleles down to 1% minor allele fraction (MAF) at a read depth of >1000x.

OGT's expert bait design ensures efficient and more uniform capture of all targeted regions than amplicon-based technologies, so that all variants present can be called with maximum confidence. This has been demonstrated on the *CALR* gene, which is commonly mutated in various MPNs. It is critical to identify key *CALR* indels (types 1 & 2 causing a frameshift) as well as increasingly recognised point mutations in this gene. The SureSeq Myeloid Panel delivers superior performance to panels designed using standard algorithms by ensuring uniform coverage over the regions of interest (Figure 1).

ASXL1	*EGLN1*	*IDH2*	*NRAS*	*SRSF2*
CBL	*EPAS1*	***JAK2***	*RUNX1*	*TET2*
CALR	*EPOR*	***KIT***	*SETBP1*	*TP53*
CSF3R	*EZH2*	*KRAS*	*SF3B1*	*U2AF1*
DNMT3A	*IDH1*	***MPL***	*SH2B3*	*VHL*

Table 1: The SureSeq Myeloid Panel targets 25 genes implicated in a variety of MPNs. The gene content has been defined with input from recognised cancer experts including Professor Mike Griffiths (West Midlands Regional Genetics Laboratory, UK) and Professor Nick Cross (National Genetics Reference Laboratory – Wessex, UK).

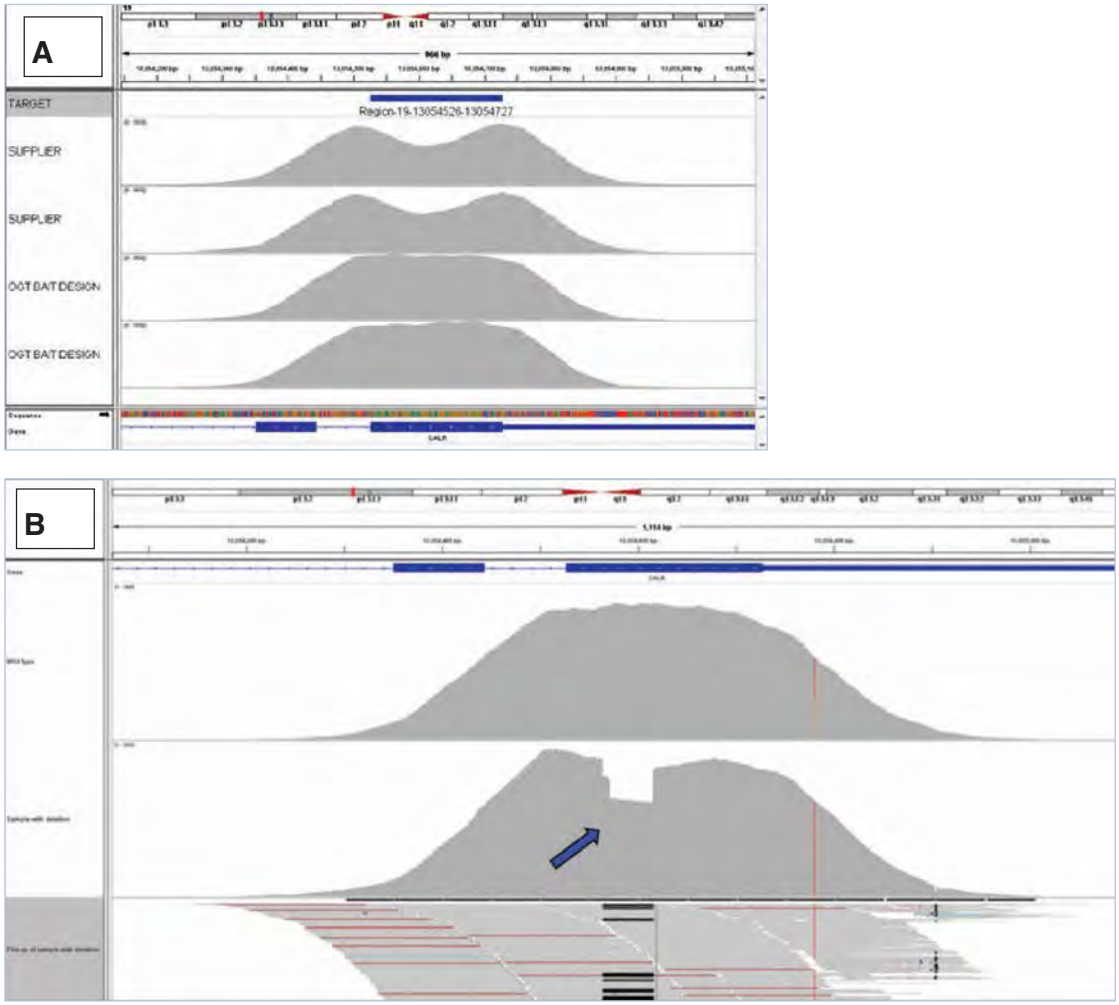


Figure 1: A) OGT's expert bait design delivers improved uniformity of coverage. Shown here is exon 9 of *CALR*. The top two captures have been completed using baits designed with standard commercially available software. They have a considerable dip in coverage in the middle of the exon due to the fact it presents a low complexity region with low nucleotide diversity. Most algorithms would want to avoid such regions in the design. However, OGT's superior bait design can increase the evenness of coverage of such regions. **B)** The top panel shows a normal control sample and the bottom panel shows 23% deletion (c.1092_1143del_52bp) in *CALR* exon 9. Mean target coverage >1000x, 24 samples per MiSeq lane.

SureSeq™

Cat. No. **600071** (16 reactions)
Cat. No. **600070** (96 reactions)

SureSeq Solid Tumour Panel

60-gene solid tumour panel allows discovery of novel and known variants in a range of solid tumours; fully validated on FFPE samples

The SureSeq Solid Tumour Panel delivers:

- Highly accurate determination of allele frequency — hybridisation-based enrichment allows the removal of PCR-based bias and duplications
- Comprehensive variant detection — targeting every codon of every exon in 60 key genes for mutation detection and discovery
- Improved coverage uniformity — sensitive and reproducible variant detection even in heterogeneous samples
- Fully validated on FFPE samples — unlock the potential of precious samples
- Powerful variant analysis software included — use OGT's user-friendly interactive report or your own analysis pipeline for flexible data analysis

Utilising hybridisation-based enrichment, the SureSeq Solid Tumour Panel delivers greater run-to-run consistency and significantly less PCR bias (Figure 1) than amplicon-based assays. Run-to-run consistency is an important metric in determining confidence in NGS analysis — inconsistency indicates that duplicate or even triplicate sequencing may be necessary to ensure confidence in the assay result. Amplicon-based enrichment is susceptible to amplification bias, particularly in situations where there is limited sample or where the ability to detect minor allele frequencies (MAF) is required (e.g. heterogeneous samples). Such bias may cause important variants to be missed or over-represented.

The SureSeq Solid Tumour Panel targets selected key genes known to contain driver mutations for a range of cancer types including breast, prostate, ovarian, lung and colorectal (Table 1). The gene content has been defined by recognised cancer experts. Targeting the entire coding regions of selected key genes, the SureSeq Solid Tumour Panel allows the discovery of novel variants as well as the analysis of known mutation hotspots.

The panel has been validated using DNA extracted from FFPE samples for a range of solid tumours, including sarcomas and lung, pancreatic and head and neck cancers (Table 2) and has been optimised to work with as little as 100–500 ng of genomic DNA from formalin-fixed, paraffin-embedded (FFPE) samples, allowing you to unlock the potential of archived samples.

In order to detect alleles that contribute only a small percentage to the reads at any locus, a highly uniform and sensitive enrichment is required. OGT's expert bait design ensures efficient and more uniform capture of all targeted regions than amplicon-based technologies, so that all variants present can be called with maximum confidence.

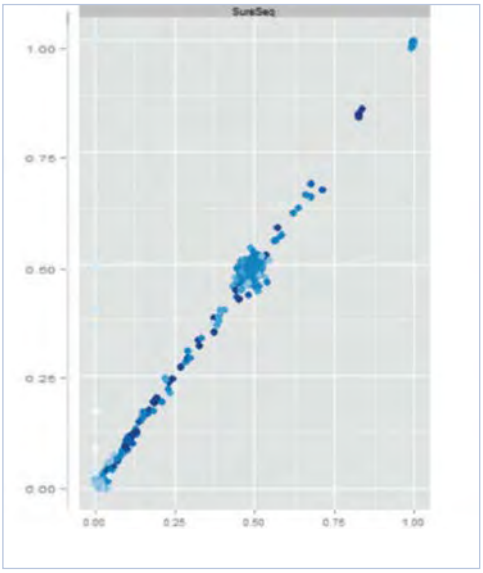


Figure 1: The hybridisation-based SureSeq Solid Tumour Panel delivers consistent, reliable results. Replicates of 3 samples were individually enriched using the SureSeq Solid Tumour Panel and subsequently sequenced. Comparison of the allele frequencies of each run showed very high concordance, demonstrating the reproducibility of the assay.

AKT1	*BRCA2*	*FGFR2*	*MAP2K1*	*NOTCH1*	*SMAD4*
ALK	*CDH1*	*FGFR3*	*MED12*	*NRAS*	*SMARCA4*
APC	*CDKN1B*	*FOXA1*	*MET*	*PDGFRA*	*SMARCB1*
AR	*CDKN2A*	*GNAS*	*MLH1*	*PDGFRB*	*SMO*
ARID1A	*CHD1*	*HRAS*	*KMT2A (MLL1)*	*PIK3CA*	*SPOP*
ASXL1	*CTNNB1*	*IDH1*	*KMT2C (MLL3)*	*PTEN*	*STK11*
ATM	*DDR2*	*JAK2*	*KMT2D (MLL2)*	*PTPN11*	*TP53*
AXL	*EGFR*	*JAK3*	*MTOR*	*RB1*	*KDM6A (UTX)*
BRAF	*ERBB2*	*KIT*	*NF1*	*RET*	*VHL*
BRCA1	*FGFR1*	*KRAS*	*NKX3.1*	*ROS1*	*ZFHX3*

Table 1: The SureSeq Solid Tumour Panel provides complete coverage of 60 key cancer genes selected by recognised cancer experts, including Cancer Research UK, Professor Mike Griffiths (West Midlands Regional Genetics Laboratory, UK) and Professor Nick Cross (National Genetics Reference Laboratory, Salisbury, UK).

Gene and variant detected	Lowest MAF observed	Gene and variant detected	Lowest MAF observed
BRAF c.1799T>A (p.Val600Glu)	7.1%	*EGFR* exon 19 deletions	6%
KRAS c.34G>T (p.Gly12Cys)	1.3%	*EGFR* exon 20 insertions	4%
KRAS c.35G>T (p.Gly12Cys)	1.2%	*FGFR3* c.742C>T p.R248C	33.3%
KRAS c.37G>T (p.Gly13Val)	1.9%	*FGFR3* c.743G>A p.R248H	2.1%
KRAS c.38G>A (p.Gly13Asp),	12.5%	*NRAS* c.181C>A p.Q61K	23.2%
KRAS c.183A>T (p.Gln61His)	5.9%	*PDGFRA* c.1432T>C p.S478P	31.5%
KRAS c.34_35del GGinsTT (p.Gly12Phe)	10%	*PTEN* c.697C>T p.R233*	1%
DDR2 c.476T>C (p.Ile159Thr)	24%	*TP53* c.743G>A p.R248Q	5.6%
EGFR c2573T>G (p.Leu858Arg)	10.7%	*TP53* c.817C>T p.R273C	1.1%

Table 2: Example mutations detected in FFPE samples from a range of solid tumours using the SureSeq Solid Tumour Panel. The ability to accurately detect MAF as low as 1.1% gives added confidence in the variants being called and facilitates the exploration of tumour heterogeneity.

SureSeq™

Provided with all SureSeq panels

SureSeq Interpret Software

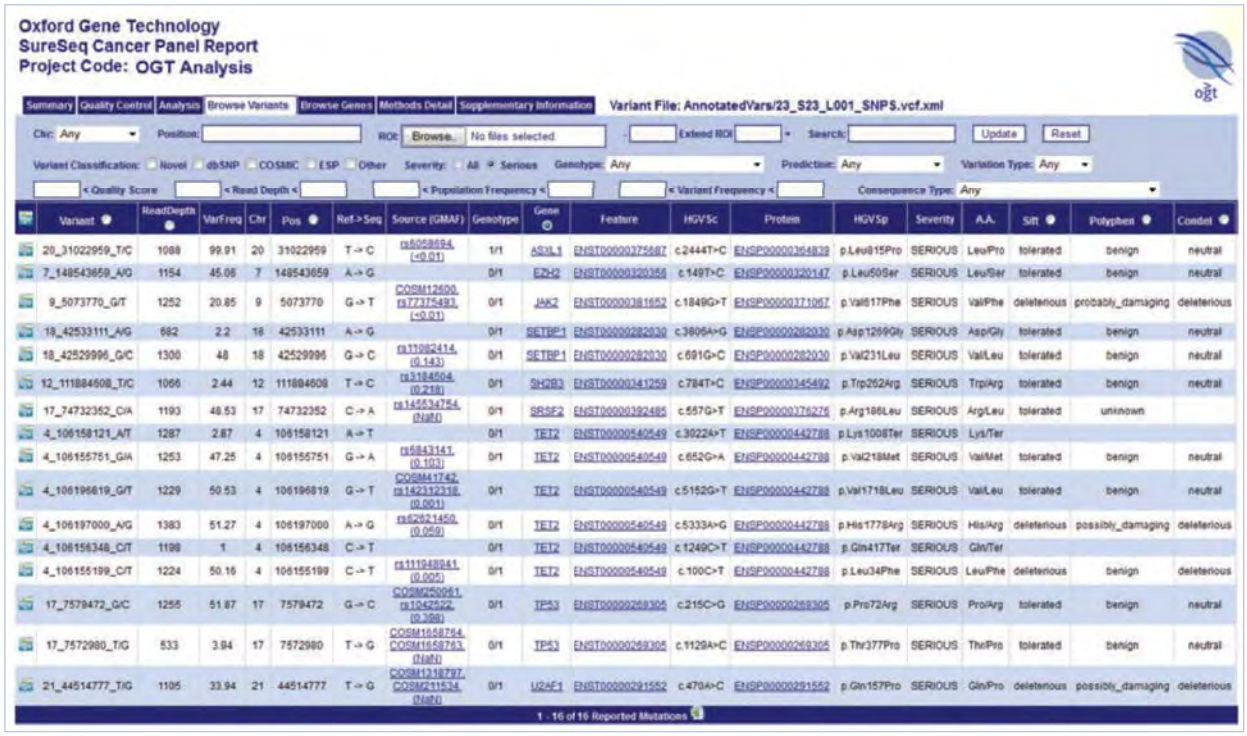
OGT's powerful stand-alone data analysis package, provided free with all SureSeq NGS panels

SureSeq Interpret Software delivers:

- Powerful bioinformatics analysis to your desktop — overcomes data privacy and handling hurdles
- User-friendly reporting to allow easy filtering of variants — no need for additional in-house bioinformatics resources
- Sensitive and reproducible variant detection even in heterogeneous samples — removal of PCR bias
- Detection of germline and somatic mutations — compatible with both cancer and molecular panels
- Results presented in context — all variants are fully annotated with links to various databases

SureSeq Interpret Software is OGT's powerful, standalone data analysis package optimised to detect low-frequency variants, even in heterogeneous samples. It allows processing of FASTQ files to deliver an intuitive interactive report. The software complements the SureSeq range of panels enabling simple yet powerful data analysis.

OGT has validated a number of analysis pipelines, tailored to specific applications, from standard germline variant detection to high-sensitivity somatic variant detection in a heterogeneous background. The unique SureSeq Interpret Software incorporates these pipelines and provides researchers with the freedom to explore and retrospectively interrogate data with additional or new selection criteria, without the need for additional in-house bioinformatics resource (Figure 1). Using the report, data can be easily filtered by numerous parameters, including gene, depth of coverage, somatic variants and predicted effect on the protein. In addition, all variants are fully annotated with links to various databases (e.g. dbSNP, COSMIC, Genecards and OMIM) providing results in context. Each variant can be reviewed in the Integrative Genomics Viewer (IGV) from the Broad Institute (Figure 2).



Oxford Gene Technology
SureSeq Cancer Panel Report
Project Code: OGT Analysis

Summary | Quality Control | Analysis | Browse Variants | Browse Genes | Methods Detail | Supplementary Information | Variant File: AnnotatedVars/23_S23_L001_SNPS.vcf.xml

Variant	ReadDepth	VarFreq	Chr	Pos	Ref->Seq	Source (GMAF)	Genotype	Gene	Feature	HGVSc	Protein	HGVSp	Severity	A.A.	Sift	Polyphen	Condel
20_31022959_T/C	1088	99.91	20	31022959	T -> C	rs6058694 (<0.01)	1/1	ASXL1	ENST00000375687	c.2444T>C	ENSP00000364839	p.Leu815Pro	SERIOUS	Leu/Pro	tolerated	benign	neutral
7_148543659_A/G	1154	45.06	7	148543659	A -> G		0/1	EZH2	ENST00000320356	c.149T>C	ENSP00000320147	p.Leu50Ser	SERIOUS	Leu/Ser	tolerated	benign	neutral
9_5073770_G/T	1252	20.85	9	5073770	G -> T	COSM12600, rs77375493 (<0.01)	0/1	JAK2	ENST00000381652	c.1849G>T	ENSP00000371067	p.Val617Phe	SERIOUS	Val/Phe	deleterious	probably_damaging	deleterious
18_42533111_A/G	582	2.2	18	42533111	A -> G		0/1	SETBP1	ENST00000282030	c.3806A>G	ENSP00000282030	p.Asp1269Gly	SERIOUS	Asp/Gly	tolerated	benign	neutral
18_42529996_G/C	1300	48	18	42529996	G -> C	rs11082414 (0.143)	0/1	SETBP1	ENST00000282030	c.691G>C	ENSP00000282030	p.Val231Leu	SERIOUS	Val/Leu	tolerated	benign	neutral
12_111884608_T/C	1066	2.44	12	111884608	T -> C	rs3184504 (0.218)	0/1	SH2B3	ENST00000341259	c.784T>C	ENSP00000345492	p.Trp262Arg	SERIOUS	Trp/Arg	tolerated	benign	neutral
17_74732352_C/A	1193	48.53	17	74732352	C -> A	rs145534754 (NaN)	0/1	SRSF2	ENST00000392485	c.557G>T	ENSP00000376276	p.Arg186Leu	SERIOUS	Arg/Leu	tolerated	unknown	
4_106158121_A/T	1287	2.87	4	106158121	A -> T		0/1	TET2	ENST00000540549	c.3022A>T	ENSP00000442788	p.Lys1008Ter	SERIOUS	Lys/Ter			
4_106155751_G/A	1253	47.25	4	106155751	G -> A	rs5843141 (0.103)	0/1	TET2	ENST00000540549	c.652G>A	ENSP00000442788	p.Val218Met	SERIOUS	Val/Met	tolerated	benign	neutral
4_106196819_G/T	1229	50.53	4	106196819	G -> T	COSM41742, rs142312316 (0.001)	0/1	TET2	ENST00000540549	c.5152G>T	ENSP00000442788	p.Val1718Leu	SERIOUS	Val/Leu	tolerated	benign	neutral
4_106197000_A/G	1383	51.27	4	106197000	A -> G	rs62621450 (0.059)	0/1	TET2	ENST00000540549	c.5333A>G	ENSP00000442788	p.His1778Arg	SERIOUS	His/Arg	deleterious	possibly_damaging	deleterious
4_106156348_C/T	1198	1	4	106156348	C -> T		0/1	TET2	ENST00000540549	c.1249C>T	ENSP00000442788	p.Gln417Ter	SERIOUS	Gln/Ter			
4_106155199_C/T	1224	50.16	4	106155199	C -> T	rs111948941 (0.005)	0/1	TET2	ENST00000540549	c.100C>T	ENSP00000442788	p.Leu34Phe	SERIOUS	Leu/Phe	deleterious	benign	deleterious
17_7579472_G/C	1255	51.87	17	7579472	G -> C	COSM250061, rs1042522 (0.398)	0/1	TP53	ENST00000269305	c.215C>G	ENSP00000269305	p.Pro72Arg	SERIOUS	Pro/Arg	tolerated	benign	neutral
17_7572980_T/G	533	3.94	17	7572980	T -> G	COSM1658764, COSM1658763 (NaN)	0/1	TP53	ENST00000269305	c.1129A>C	ENSP00000269305	p.Thr377Pro	SERIOUS	Thr/Pro	tolerated	benign	neutral
21_44514777_T/G	1105	33.94	21	44514777	T -> G	COSM1318797, COSM211534 (NaN)	0/1	U2AF1	ENST00000291552	c.470A>C	ENSP00000291552	p.Gln157Pro	SERIOUS	Gln/Pro	deleterious	possibly_damaging	deleterious

1 - 16 of 16 Reported Mutations

Figure 1: The SureSeq Interpret Report enables simple and rapid identification of meaningful results.

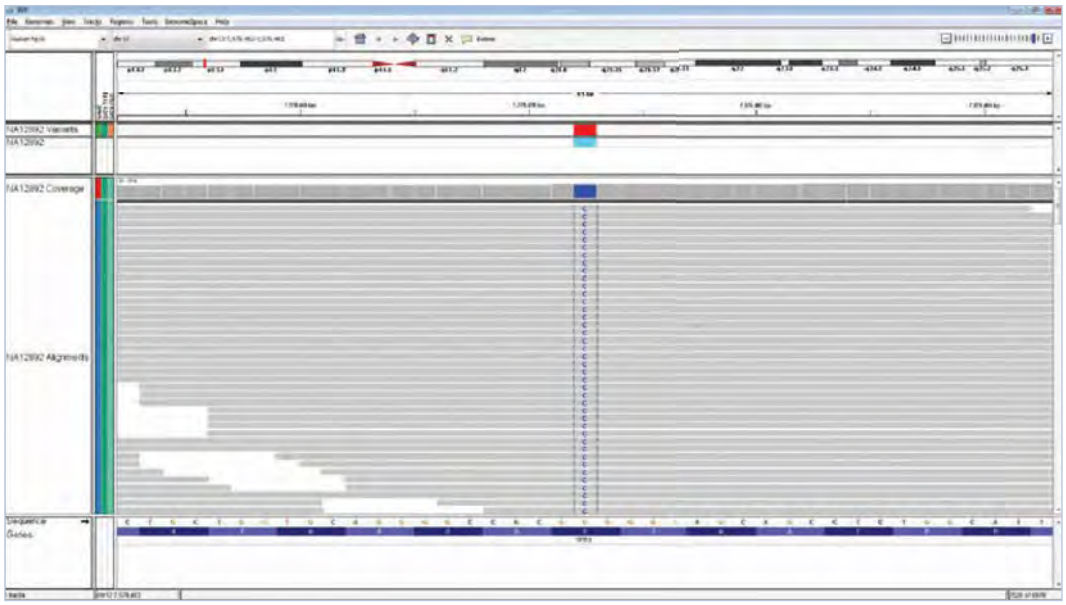
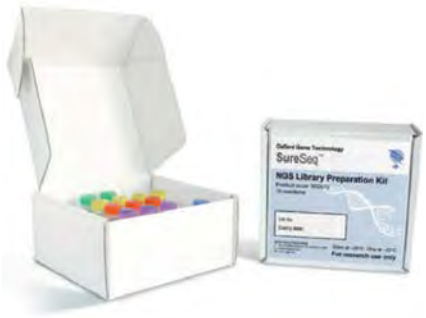


Figure 2: Fast visual confirmation of variants using IGV from the Broad Institute.

SureSeq™

Cat. No. **500070** (16 reactions)
Cat. No. **500073** (48 reactions)

SureSeq NGS Library Preparation Kit



Streamlined library preparation for industry-leading next generation sequencing (NGS) results

The SureSeq NGS Library Preparation Kit delivers:

- Greater trust in your data — high performance with low duplication rates, high sequence quality and high percentage of on-target bases
- Faster process — streamlined protocol reduces manual handling steps to save time, increasing reliability as well as throughput
- Reliable results — targeted panel, library preparation and powerful analysis software are fully optimised for perfect results every time

Streamlined protocol for a faster process

The SureSeq NGS Library Preparation Kit generates NGS libraries suitable for the capture of targeted genomic regions using hybridisation. Optimisation of enzymes and buffers enables the number of steps to be minimised, while still delivering libraries of the highest quality. The kit contains the reagents required to prepare an NGS library including, Illumina sequencing platform specific adaptor sequences, PCR primers, enzymes, and indexes.*

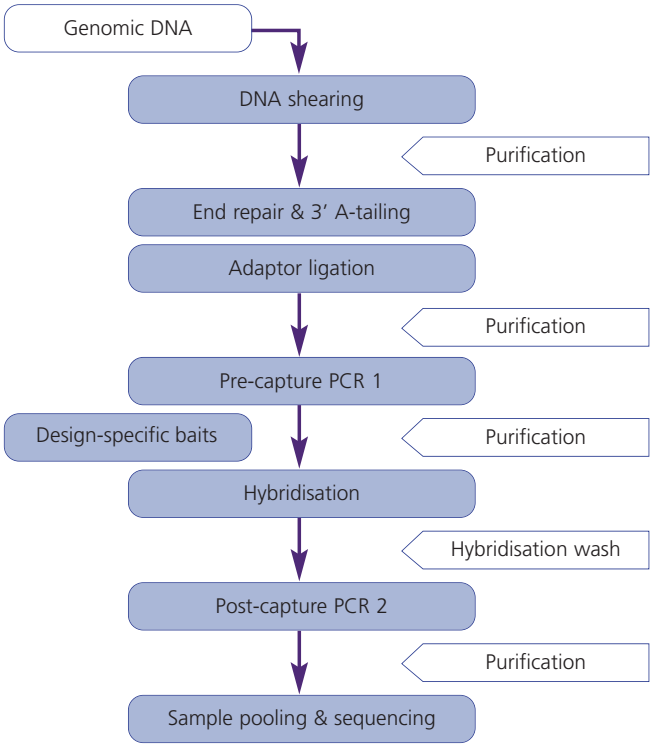


Figure 1: A streamlined protocol, including enrichment by hybridisation. The complete procedure can be completed in 1.5 days with minimal handling time.

* Requires hybridisation and wash buffers; sold separately.

By extensive testing of enzymes and buffer optimisation, it has been possible to streamline the standard library preparation protocol to reduce the number of hands-on steps and the overall processing time (Figure 1).

- End repair and ligation are combined into a single step
- Number of purification steps, where material is lost, is reduced
- Fewer steps reduce handling errors for increased reliability
- Reduced technician cost and increased sample throughput

High-quality data generation

NGS data is increasingly being relied upon as a front line technology for the generation of data for scientific and medical research. A combination of quality metrics are used to give confidence that variants called are real and the number of false positive calls are low. The SureSeq NGS Library Preparation Kit delivers high performance in the quality metrics that really matter, giving more reliable, more trustworthy data.

High duplication rates reduce the complexity of your NGS library and can lead to poor coverage of target genomic regions even though average coverage rates appear high. The SureSeq NGS Library Preparation Kit gives exceptionally low levels of duplication (Figure 2), ensuring the complexity of the library is maintained, with more even coverage and high levels of confidence in the data produced.

High levels of on-target bases are required to maximise the amount of useful information obtained from a given sequencing lane. This leads to increased sequence complexity and greater depth of coverage of the target regions.

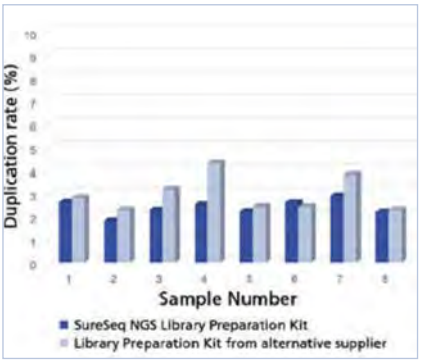


Figure 2: The SureSeq NGS Library Preparation Kit delivers low levels of sequence duplication. The duplication rates are shown for 8 samples sequenced using exome capture (Agilent SureSelect Human All Exon V5) with the SureSeq NGS Library Preparation Kit and a library preparation kit from an alternative supplier.

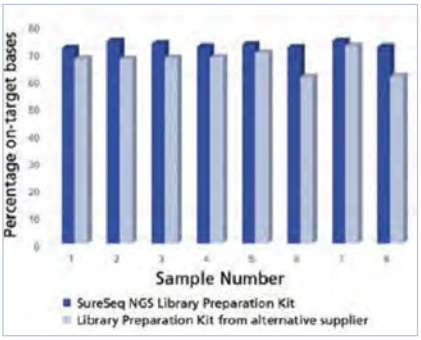


Figure 3: High percentage of on-target bases. The percentage of on-target bases are shown for exome capture (Agilent SureSelect Human All Exon V5) using the SureSeq NGS Library Preparation Kit and a library preparation kit from an alternative supplier.

SureSeq™

Cat. No. **500079** (16 reactions)

SureSeq FFPE DNA Repair Mix

SureSeq FFPE DNA Repair Mix:

- Optimised to repair a broad range of damage in FFPE-derived DNA — remove artefacts caused by fixation and long-term storage
- Improves NGS library yields, %OTR and mean target coverage — get excellent sequencing data for confident variant calling from FFPE DNA
- Allows decreased amount of input DNA — preserve your precious samples and get meaningful results from as little as 100 ng of FFPE DNA

Tissue biopsies are typically archived as formalin-fixed, paraffin-embedded (FFPE) blocks, which preserve tissue morphology and allow long-term storage at room temperature. However, the methods used for fixation significantly damage and compromise the quality of nucleic acids from these samples. Consequently, it may be difficult to distinguish between true and damage-induced low-frequency mutations in such samples. SureSeq FFPE DNA Repair Mix is a mixture of enzymes that has been optimised to remove a broad range of damage that can cause artefacts in sequencing data (Table 1).

Damage	Repaired?
Deamination of cytosine to uracil	✓
Nicks and gaps	✓
Oxidised bases	✓
Blocked 3′ ends	✓
DNA fragmentation	✗
DNA-protein crosslinks	✗

Table 1: The SureSeq FFPE DNA Repair Mix is capable of removing a variety of DNA damage caused by fixation and long-term storage.

SureSeq FFPE DNA Repair Mix has been shown to significantly improve NGS library yields, preserving original complexity and delivering high-quality sequencing data for confident calling of variants with low minor allele fractions (MAFs). It also increases depth of coverage and %OTR improving sensitivity of your test (Figure 1).

Pathology labs often have to work with very limited amounts of material. Additionally, FFPE samples are usually irreplaceable. This leads to the need to reduce DNA input in downstream applications including NGS. Often amplicon-based approaches are chosen as they require very little input material. Unfortunately, due to PCR bias and lower complexity from smaller input amounts, these methods are not well suited to detect low-frequency mutations in heterogeneous tumour samples. Hybridisation-based approaches eliminate the problem of PCR bias providing much more reliable data but they typically require higher DNA inputs of 500 ng – 1 µg. Using the SureSeq FFPE DNA Repair Mix a reduction in the amount of starting material down to 100 ng depending on required depth of coverage is possible.

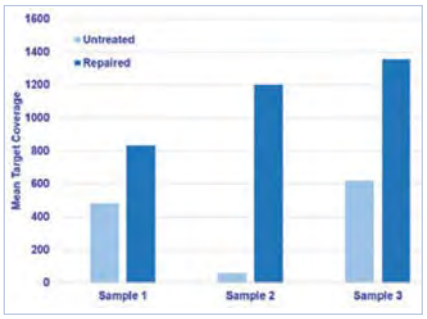


Figure1: The SureSeq FFPE DNA Repair Mix significantly improves mean target coverage resulting in more confident calls. Data obtained using 500ng of FFPE DNA from ovarian and colon cancer samples; 16 samples per MiSeq lane.

CytoSure™

Array Products

Contents

Overview

For a number of years, microarrays have been considered the first approach for research into copy number variation (CNV) and loss of heterozygosity (LOH) analysis in constitutional and cancer samples. This technique has enabled cytogenetic researchers to identify significantly more CNV and other structural alterations compared to traditional techniques such as karyotyping.

The CytoSure™ range of microarrays provide a comprehensive choice of array formats for research into constitutional and molecular disorders, cancer and pre-implantation genetic screening (PGS). Offering genome-wide coverage, many of the CytoSure arrays are also exon focused to allow detection of microdeletions and duplications at exon-level resolution. Probe design and optimisation is critical and OGT's probe design algorithms are now so sophisticated, our Oligome™ database has grown significantly to ~26.5 million optimised probes which have been screened for homologies and secondary structures, ranked and only then included in the probe database. The Oligome is a source of well curated and constantly re-evaluated probes that support and enable the development of high-quality array designs ensuring delivery of the best possible CNV and LOH detection calls. Our custom array design service allows you to quickly and efficiently benefit from our team's extensive array design expertise, and all our array products include our class-leading CytoSure Interpret™ software for fast and simple interpretation of your data.

CytoSure™ Constitutional v3: Cat. No. **020045** (8x60k), **020046** (4x180k)
Constitutional v3 +LOH: Cat. No. **020047** (4x180k)

CytoSure Constitutional v3 Arrays

Enhanced exon-level coverage of developmental disorder genes and the latest ClinGen* and DDD content

The CytoSure Constitutional v3 arrays deliver:

- The most up-to-date developmental disorder content — all the latest research-validated genes and regions
- Single exonic CNV detection in the genes that matter — enabling high-resolution CNV detection in up to 502 genes of interest
- Integrated sample tracking probes and optimised labelling kits — the complete solution for reliable analysis and reporting
- Streamlined data analysis and interpretation — straightforward and fast analysis of CNVs and LOH

Enhanced exon-level coverage of all developmental disorders and the latest ClinGen and DDD content

CytoSure Constitutional v3 arrays have been developed in collaboration with experts at the Wellcome Trust Sanger Institute. These unique arrays combine the most up-to-date and relevant developmental delay content from the recent Deciphering Developmental Disorders (DDD) study with the latest updates from ClinGen the Clinical Genome Resource[1].

Higher probe density across the exons and introns of important developmental delay genes allows improved detection of small (<500bp) deletions and duplications that might otherwise be missed or require manual calling on other constitutional cytogenetics array designs (Figures 1 and 2). An informed, sophisticated approach to array design has been used, with more probes being located in regions of the genome that are most likely to detect a biologically relevant aberration (Table 1). The addition of a research-validated collection of single nucleotide polymorphism (SNP) probes on the CytoSure Constitutional v3 +LOH arrays facilitates the precise identification of loss of heterozygosity (LOH) and uniparental disomy (UPD) in addition to accurate copy number (CN) detection.

Streamlined data analysis and interpretation

CytoSure Interpret Software, provided free of charge with all CytoSure arrays, is a powerful, easy-to-use package for the analysis of CNV and SNP data which includes a host of innovative features to enable the automation of data analysis workflows, for more information see page 206.

CytoSure Constitutional v3 arrays are available in a range of formats to match your resolution and throughput requirements. All CytoSure arrays have been research-validated using CytoSure Genomic DNA Labelling Kits, for more information see page 208.

REFERENCES

1. NCBI (2015) ClinGen Dosage Sensitivity Map [online] Available from: http://ncbi.nlm.nih.gov/projects/dbvar/clingen [Accessed 28 May 2015]

*Formerly known as ISCA/ICCG.

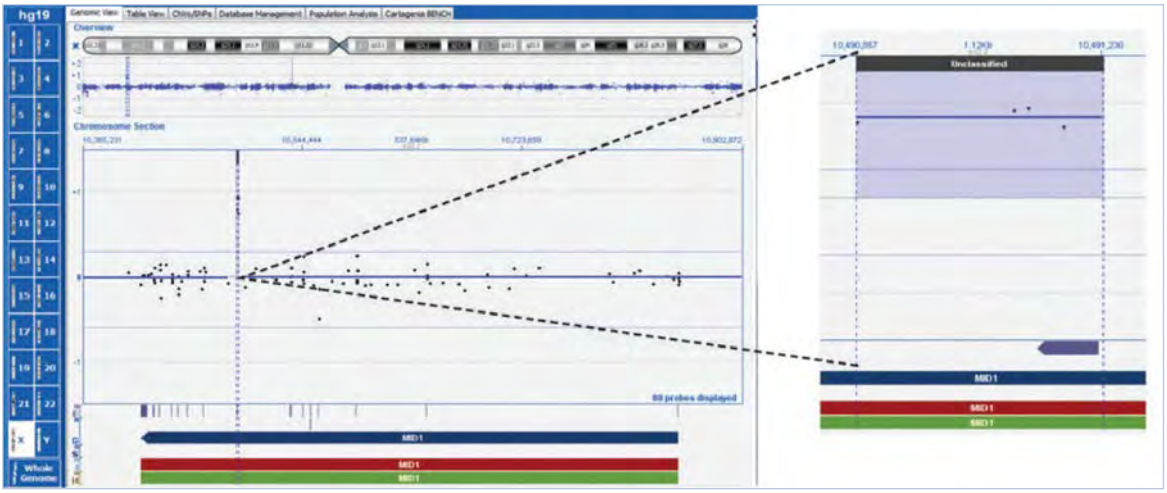


Figure 1: Accurate detection of a small, single-exon (<500bp; 4 probes) duplication in *MID1* associated with Opitz-G syndrome.*

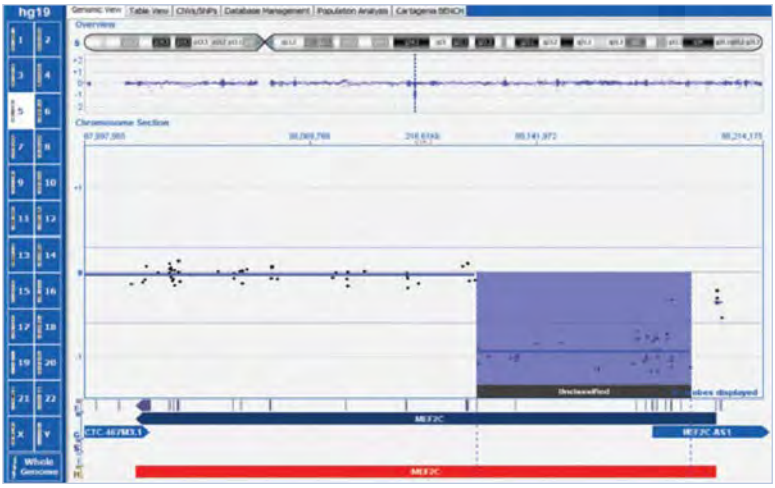


Figure 2: Enhanced probe coverage. A 68kb deletion covering *MEF2C* gene. The CytoSure Constitutional v3 8x60k array contains 36 probes in this region. This deletion was previously called manually on the CytoSure ISCA v2 8x60k array which has only 2 probes in this deletion.*

* Data kindly provided by by West Midlands Regional Genetics Laboratories (WMRGL), Birmingham, UK. Find out more at www.ogt.com/cytosure

	Format	Cat. no.	Top priority genes	Medium priority genes	Lower priority genes	Decipher Syndrome regions	ClinGen regions	High priority backbone resolution	Medium priority backbone resolution	Low priority backbone resolution	LOH resolution
CytoSure Constitutional v3	8x60k	020045	Exon targeted	Whole-gene targeted	Whole-gene targeted	Whole-gene targeted	Whole-gene targeted	189kb	375kb	663kb	-
CytoSure Constitutional v3	4x180k	020046	Exon targeted	Exon targeted	Exon targeted	Whole-gene targeted	Whole-gene targeted	68kb	74kb	162kb	-
CytoSure Constitutional v3 +LOH	4x180k	020047	Exon targeted	Whole-gene targeted	Whole-gene targeted	Whole-gene targeted	Whole-gene targeted	68kb	74kb	162kb	7Mb and above

Table 1: Selection guide for CytoSure Constitutional v3 arrays. For a complete list of genes covered, please email: products@ogt.com

CytoSure™

ISCA v2: Cat. No. **020042** (4x44k), **020040** (8x60k), **020041** (4x180k)

ISCA v2 +SNP: Cat. No. **020052** (8x60k), **020051** (4x180k)

ISCA UPD: Cat. No. **020050** (4x180k)

CytoSure ISCA Arrays

A range of optimised arrays designed in collaboration with the International Standards for Cytogenomic Arrays (ISCA) Consortium

CytoSure ISCA and ISCA +SNP arrays deliver:

- Accurate detection of CN and LOH on a single array*
- Gold-standard detection of CN changes with complete coverage of the ISCA regions
- A range of array formats to suit your requirements
- Easy identification of sample mix-up via spike-in controls
- Fast and easy data generation and interpretation

CytoSure ISCA and ISCA +SNP arrays deliver standardised, evidence-based designs to the cytogenetics research community, focusing on disease and syndrome-associated genome regions, in addition to offering whole genome 'backbone' coverage.

The CytoSure ISCA +SNP array combines long oligo array comparative genome hybridisation (aCGH) probes for superior copy number variation (CNV) detection with fully research-validated single nucleotide polymorphism (SNP) content for accurate identification of loss of heterozygosity (LOH) and uniparental disomy (UPD). This enables cost-effective identification of a broader range of genetic syndromes in a single array experiment — without any additional investment in equipment or training.

Streamlined Data Analysis and Interpretation

CytoSure Interpret Software, provided free of charge with all CytoSure arrays, is a powerful, easy-to-use package for the analysis of CNV and SNP data which includes a host of innovative features to enable the automation of data analysis workflows, for more information see page 206.

CytoSure Constitutional ISCA and ISCA +SNP arrays are available in a range of formats to match your resolution and throughput requirements. All CytoSure arrays have been research-validated using CytoSure Genomic DNA Labeling Kits, for more information see page 208.

*CytoSure ISCA +SNP and ISCA UPD only.

Application	Product Name	Format	Cat. No.	Copy number (CN) resolution		Loss of heterozygosity (LOH) resolution
				Targeted	Backbone	
Whole genome CN screening, plus high coverage of ISCA defined regions	CytoSure ISCA v2 CytoSure ISCA v2 CytoSure ISCA v2	4x44k 8x60k 4x180k	020042 020040 020041	1 probe every 52kb 1 probe every 48kb 1 probe every 19kb	1 probe every 81kb 1 probe every 70kb 1 probe every 25kb	NA
Whole genome CN and LOH screening, plus CN coverage of ISCA defined regions	CytoSure ISCA +SNP	8x60k	020052	1 probe every 80kb	1 probe every 141kb	30Mb
Whole genome CN screening and UPD, plus high res. CN coverage of ISCA defined regions	CytoSure ISCA UPD	4x180k	020050	1 probe every 20kb	1 probe every 27kb	30Mb
Whole genome CN and LOH, screening plus high res. CN coverage of ISCA defined regions	CytoSure ISCA +SNP	4x180k	020051	1 probe every 48kb	1 probe every 70kb	7-10Mb

Table 1: CytoSure ISCA and ISCA +SNP Selection Guide. For a complete list of genes covered email: products@ogt.com

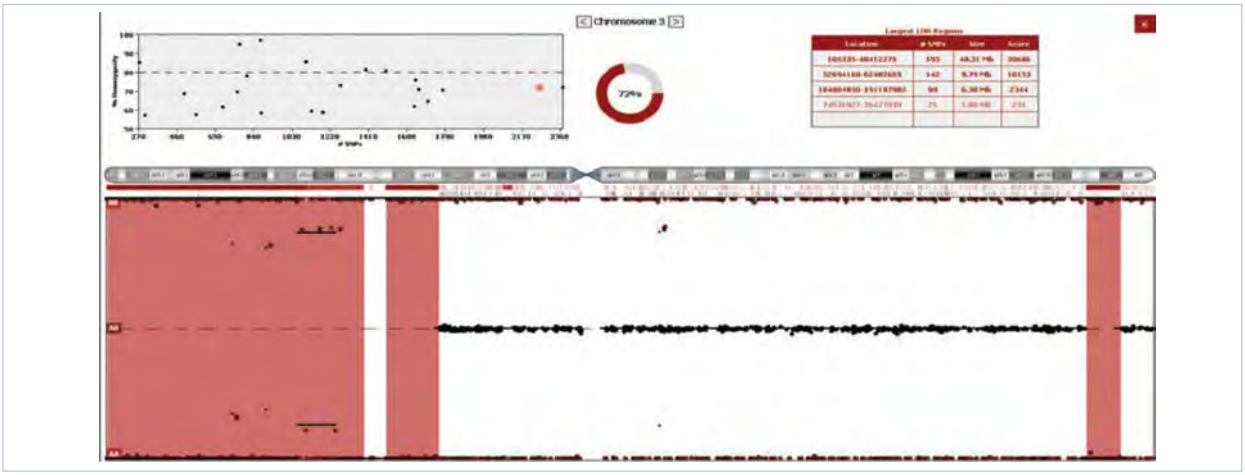


Figure 1: CytoSure Interpret Software clearly displays the percentage of homozygous and heterozygous SNPs for each chromosome. The position of the SNP probes is shown beneath the chromosome image. Red lines indicate homozygous alleles, black heterozygous. Continuous stretches of homozygous alleles, indicating regions of LOH are shown by red rectangles. The details of these regions are also tabulated. To define the genotype of each SNP, the data is segmented using the individual BAF scores and the Circular Binary Segmentation (CBS) algorithm. Following segmentation each SNP is assigned a state which is then displayed in the Allele Status Plot. Chromosome 3 data from a consanguineous sample where regions of LOH of 48.31Mb, 9.79Mb and 6.38Mb have been detected.*

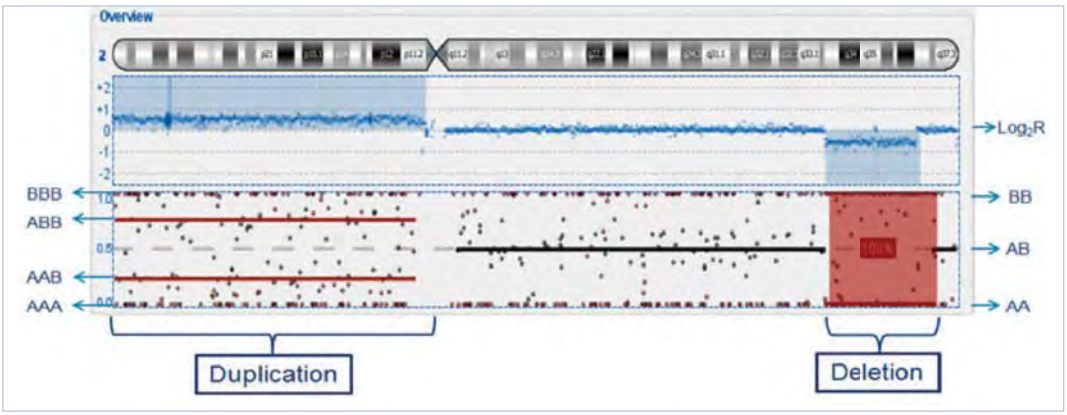


Figure 2: CytoSure Interpret Software displays changes in copy number alongside regions where LOH has been detected. This aids interpretation of complex aberrations. All data generated using the CytoSure ISCA +SNP (4x180k) array.**

* Data kindly provided by Emory Genetics.

** Data kindly provided by Prof. Joris Vermeesch and Simon Ardui, Centre of Human Genetics, KU Leuven.

CytoSure™ products are for research use only, not for use in diagnostic procedures.

CytoSure™ Cat. No. **020044** (8x60k)

CytoSure Embryo Screen Array

Reliable screening of aneuploidies and aberrations in amplified DNA extracted from single cells

CytoSure Embryo Screen array delivers:

- Confident genome-wide aneuploidy detection in pre-implantation research
- Optimised data analysis tailored for easy identification of large aberrations
- Multiplex format allows reliable processing of up to fourteen samples on a single slide

Confident genome-wide aneuploidy detection

The CytoSure Embryo Screen array utilises long oligo array comparative genomic hybridisation (aCGH) for superior aneuploidy and copy number detection. The array content has been optimised to work with small amounts of DNA amplified from a single cell, specifically single cells isolated from a pre-implantation embryo. The complimentary, industry-leading CytoSure Interpret Software allows intuitive, single-click data analysis (Figure 1).

Current molecular techniques for pre-implantation genetic screening (PGS) such as traditional fluorescence *in situ* hybridisation (FISH) and bacterial artificial chromosome (BAC)-based CGH arrays have a number of limitations that are successfully overcome using the CytoSure Embryo Screen array. The CytoSure Embryo Screen array allows the detection of aneuploidies across the whole genome and provides lower batch to batch variation, enabling more reliable analysis, plus flexibility in design and content, which further enhances their utility to meet any future research requirements. For optimum performance, the array can be combined with the CytoSure Genomic DNA Labelling Kit, which offers high signal intensities and an excellent signal-to-noise ratio, for more information see page 208.

Multiplex format allows reliable processing of up to fourteen samples on a single slide

Research into the chromosomal content of pre-implantation embryos is typically done with multiple samples. The CytoSure Embryo Screen array can be set up to suit all laboratory throughput requirements. The low-throughput option requires preparation of eight test and eight reference samples (Figure 2), with the data analysed using standard two-colour hybridisation. Alternatively, for high-throughput requirements, a single-channel approach can be utilised, enabling fourteen samples to be analysed on a single array slide. This flexible approach increases processing efficiency and cost effectiveness as greater multiplexing reduces the number of slides required, minimising both reagents used and handling time.

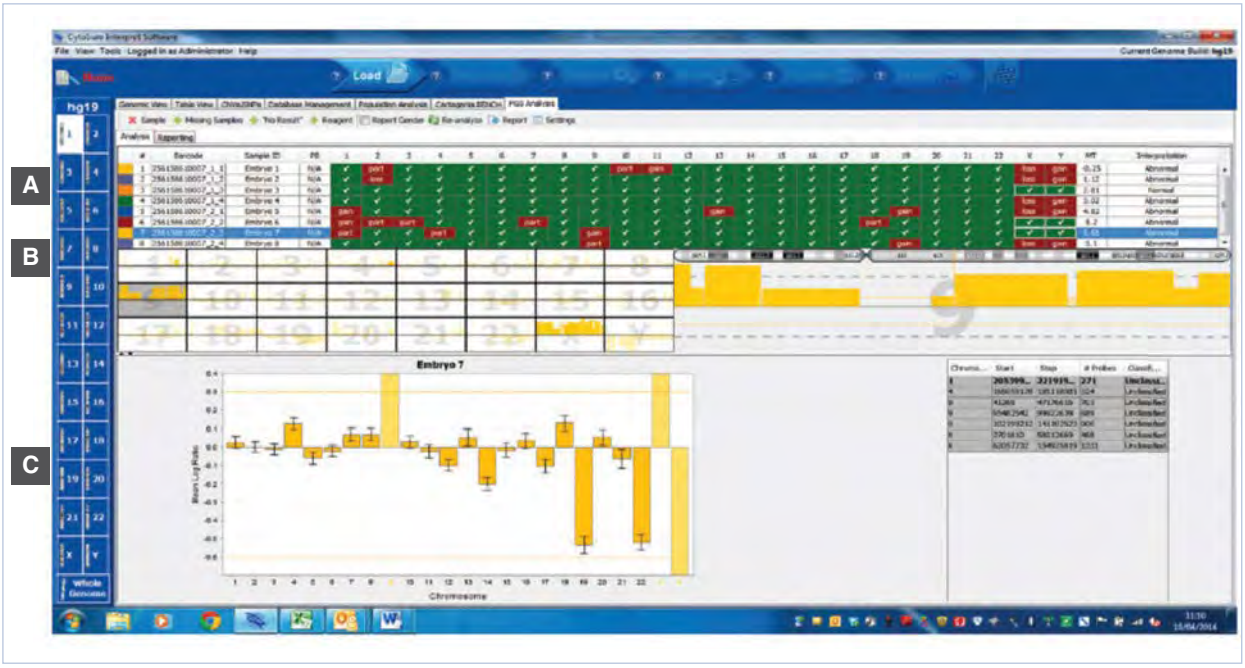


Figure 1: The CytoSure Embryo Screen array in combination with CytoSure Interpret Software enables easy and accurate detection of aberrations. Data obtained from amplified DNA extracted from single pre-implantation embryo cells: a summary of multiple results highlighting the gains and losses in each chromosome **A**, selecting a sample in the table displays it in the chromosome overview table **B** and aneuploidy summary plot **C**. The female sample shown here has a gain of chromosome 9*.

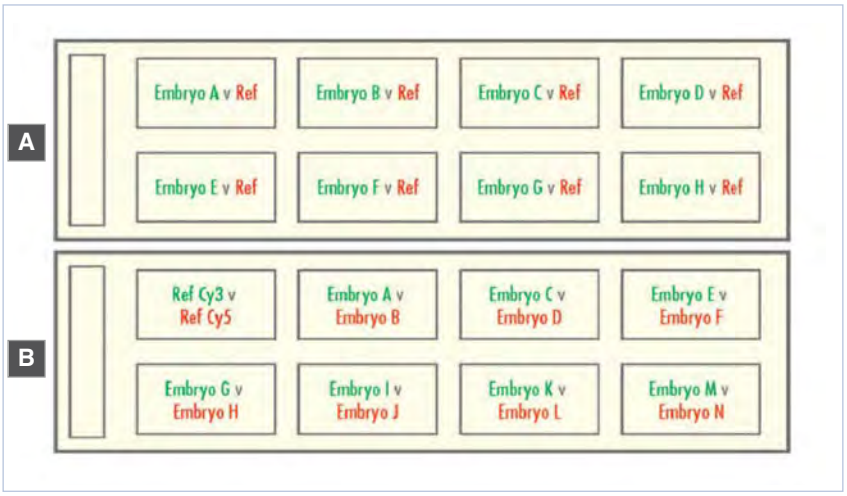


Figure 2: Reliable and cost-effective sample processing. The CytoSure Embryo Screen array can be set-up to run **A** eight samples or **B** fourteen samples to suit any throughput requirements. Red text indicates that the sample has been labelled in Cy-5 and green text indicates it has been labelled using Cy-3.

*Samples were kindly provided by Cindy Melotte, Eftychia Dimitriadou and Joris R. Vermeesch, Center for Human Genetics, University Hospital Leuven, Department of Human Genetics, KU Leuven, Belgium.

CytoSure™ Cat. No. **020100** (1x1M)

CytoSure Medical Research Exome Array

Complete coverage of all medically relevant genes; ultra-high resolution, exon-focused CNV calling in inherited molecular disease

CytoSure Medical Research Exome array delivers:

- Highly targeted optimised probes — detect single or multiple exonic CNVs
- Medical research relevant content — over 4600 hand-curated, research-validated genes
- Optimised labelling kits and integrated sample tracking probes — for confident analysis and reporting
- Combine with NGS exome analysis — comprehensive mutation spectrum analysis in rare disease

The CytoSure Medical Research Exome Array is a highly targeted exon-focused array capable of detecting medically relevant microdeletions and microduplications. Developed in collaboration with leading molecular genetics experts at Emory University, this array covers the most medically relevant regions of the genome gathered from their research into molecular disorders. The Medical Research Exome Array makes an ideal complement to an exome sequencing approach to provide a comprehensive mutation spectrum analysis in rare disease.

Highly targeted optimised probes

All probes were tested *in silico* and scored on quality before the highest scoring probes were printed on an array and tested in the laboratory. Only the most accurate, best performing probes were used in the final design. Probes have been selected to target the exonic regions of 4,645 genes. For the majority of genes there are a minimum of 4 probes per exon. For very large exons, probes are distributed evenly along the exon with 1 probe every 125bp. For any array design, good backbone coverage is important to ensure accurate normalisation. In the untargeted backbone, the CytoSure Medical Research Exome array has one probe every 42kb. Industry-leading coverage levels have been achieved with this design process — 88% of genes have 100% coverage, with 98% of genes having >75% coverage.

All probes in the Medical Research Exome Array can be used to create customised, high value, disease-specific arrays in multiplex formats (see page 204). Emory University has used this approach to create disease-specific arrays, each of which is also available as a catalogue product (see pages 198-200).

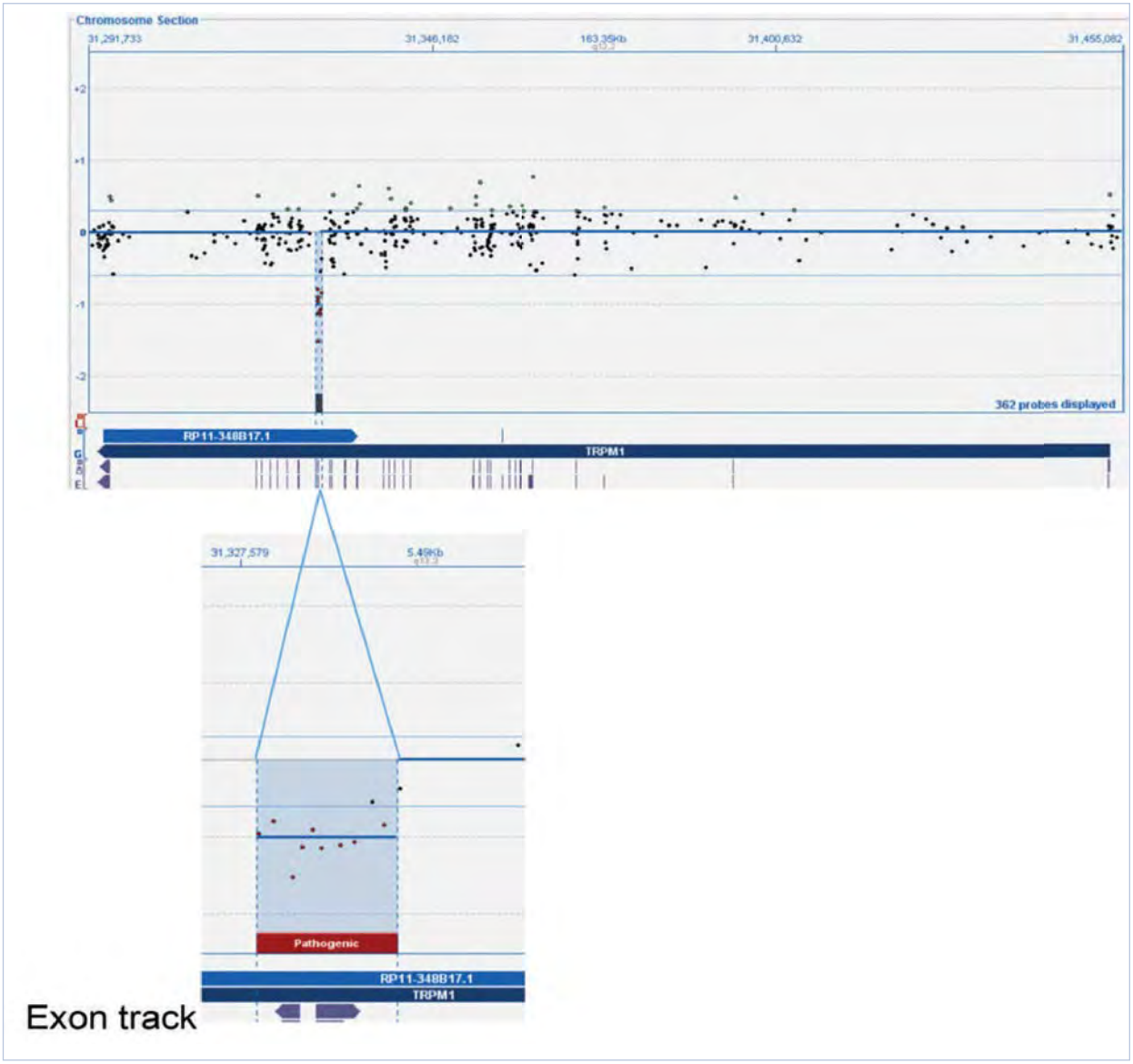


Figure 1: CytoSure Interpret Software clearly displays small aberrations and enables easy identification of genes and exons. Mutations in TRPM1 may be associated with congenital stationary night blindness. Shown here in the top panel is an overview of the whole gene. In the bottom panel, the close-up view shows a very small 684bp deletion which contains 10 probes, and also spans a single exon*.

* Data kindly provided by Madhuri Hegde, Ph.D., FACMG, Emory University.

CytoSure™

CytoSure Disease-Focused Arrays

Ultra-high resolution, exon-focused CNV calling for specific inherited molecular disease.

CytoSure Disease-Focused arrays deliver:

- Accurate detection of copy number variation at the exon level — a perfect complement to sequencing analysis
- Array content taken from the Medical Research Exome Array — fully optimised and research-validated by Emory University
- Multiplex (4x180k) format is cost-effective and allows for higher sample throughput
- Easy data interpretation using optimised protocols for high signal-to-noise ratios and industry-leading CytoSure Interpret Software

Array content fully optimised and research-validated

CytoSure disease-focused research arrays are designed to accurately identify small intragenic copy number variations (CNVs). They are exon-focused, high-resolution, 4x180k aCGH (array comparative genomic hybridisation)-based CNV array designs covering medically-relevant genes for research into specific disorders. The content for the disease focused research arrays has been designed and optimised in collaboration with leading molecular genetics experts at Emory University.

For the best results, combine the CytoSure disease-focused arrays with the CytoSure Genomic DNA labelling kits (page 208) and CytoSure Interpret Software (page 206).

Disease-focused arrays include:

- CytoSure NMD Research Array
- CytoSure Cardiomyopathy Research Array
- CytoSure Epilepsy Research Array
- CytoSure Eye Disease Research Array

CytoSure™ Cat. No. **700117** (4x180k)

CytoSure NMD Research Array

It is estimated that around 16/10,000 population are affected by some form of neuromuscular disease[1]. The CytoSure NMD (neuromuscular disease) Research array is focused primarily on the muscular dystrophies. In the most common form of muscular dystrophy, Duchenne muscular dystrophy, between 60% and 75% of disease relevant mutations are CNV[2].

- 205 genes covered
- Examples of diseases covered by the array:
  - DMD (Duchenne muscular dystrophy)
  - Limb girdle MD
  - CMD (Congenital muscular dystrophy)
  - Emery-Dreifuss MD
  - Congenital disorders of glycosylation
  - MODY (Maturity onset diabetes of the young)

REFERENCES

1. Deenen, J.C.W. *et al* (2015) The Epidemiology of Neuromuscular Disorders: A Comprehensive Overview of the Literature. Journal of Neuromuscular Disease 2(1) 73-85
2. Prior, T.W. and Bridgeman, S.J. (2005) Experience and Strategy for the Molecular Testing of Duchenne Muscular Dystrophy. J Mol Diagn. 7(3) 317-26

CytoSure™ Cat. No. **700110** (4x180k)

CytoSure Cardiomyopathy Research Array

CNV are associated with a number of cardiomyopathies, including Long QT syndrome (LQTS)[1,2] and dilated cardiomyopathy (DCM)[3], so it is important to include CNV into any research. The array includes genes that cause genetic syndromes with cardiomyopathy as a feature (e.g. Duchenne/ Becker MD, Emery-Dreifuss MD).

- 223 genes covered
- Examples of diseases covered by the array:
  - Cardiomyopathies including LQTS (Long QT syndrome), DCM (dilated cardiomyopathy), LVNC (left ventricular non-compaction)
  - Hereditary neuropathies
  - Connective tissue disorders

REFERENCES

1. Eddy, C.A. *et al.* (2008) Identification of large gene deletions and duplications in KCNQ1 and KCNH2 in patients with long QT syndrome. Heart Rhythm 5, 1275 -1281
2. Tester, D.J. *et al.* (2010) Prevalence and spectrum of large deletions or duplications in the major long QT syndrome-susceptibility genes and implications for long QT syndrome genetic testing. Am J Cardiol 106,1124 -1128
3. Norton, N. *et al.* (2011) Genome-wide studies of copy number variation and exome sequencing identify rare variants in bag 3 as a cause of dilated cardiomyopathy. Am J Hum Genet. 88, 273-82

CytoSure™ Cat. No. **700112** (4x180k)

CytoSure Epilepsy Research Array

While over 200 single-gene defects have been described in epilepsy[1], CNVs also play a key role in this disease. A recent study identified 437 CNVs in 323/805 (40%) individuals with epilepsy (1–4 per patient) ranging from 18kb to 142Mb in size[2], many of which were associated with the disease.

- 212 genes covered
- Examples of diseases covered by the array:
  - Epilepsy
  - Brain malformations
  - SCID (severe combined immune deficiency)

REFERENCES

1. Kumar, D. ed. (2008) Genomics and clinical medicine. Oxford: Oxford University Press. p. 279.
2. Olson, H. et al (2014) Copy number variation plays an important role in clinical epilepsy. Annals of Neurology 75(6), 943–958

CytoSure™ Cat. No. **700121** (4x180k)

CytoSure Autism Research Array

Autism spectrum disorders (ASD) affect 21.7 million people globally[1]. CNV linked to ASD have been described at 11 loci across 8 chromosomes[2], hence understanding CNV status is critical for research into the genetic basis of this disease.

- 227 genes covered
- Diseases covered by the array:
  - Autism
  - Hearing loss
  - XLID (X-linked intellectual disability)

REFERENCES

1. Global Burden of Disease Study 2013 Collaborators (2015). Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 386 (9995), 743-800
2. Menasha, I. et al (2013) Prioritization of Copy Number Variation Loci Associated with Autism from AutDB–An Integrative Multi-Study Genetic Database. PLOS one 8 (6), e66707

CytoSure™ Cat. No. **700113** (4x180k)

CytoSure Eye Disease Research Array

The CytoSure Eye Disease Research Array includes genes important for syndromic and non-syndromic inherited retinal and choroidal dystrophies, as well as ocular developmental disorders

- 221 genes covered
- Examples of diseases covered by the array:
  - Retinitis pigmentosa
  - Stargardt disease
  - Congenital stationary night blindness
  - Usher syndrome

CytoSure™

Other disease-focused research arrays

Other disease focused arrays are also available including arrays focused on:

- Ciliopathies 4x180k
- Metabolic disorders 4x180k
- Skeletal dysplasia 4x180k
- Hereditary cancer 4x180k
- Duchenne muscular dystrophy (DMD) 8x60k

CytoSure™

Haematological cancer +SNP: Cat. No. **020070** (8x60k)
Cancer +SNP: Cat. No. **700090** (4x180k)
Consortium Cancer +SNP: Cat. No. **020071** (4x180k)

CytoSure Cancer Arrays

Reliable detection of copy number changes and loss of heterozygosity on a single array for haematological malignancies and solid tumours

CytoSure Cancer +SNP arrays deliver:

- Confident detection of CNV and LOH on a single array
- High signal-to-noise ratios
- Flexible choice of reference sample allowing comparison of matched cancer and “normal” samples
- Exclusive CytoSure Interpret Software to translate data into meaningful results

CytoSure Cancer +SNP arrays combine aCGH (array comparative genomic hybridisation)-based CNV detection with fully research-validated SNP content allowing confident and cost-effective CNV and LOH identification using a single array (Figure 1). Due to the unique design of the SNP probes where an intensity-based comparison is made between the two SNP alleles there are no changes to the standard aCGH protocol, no restriction digest is required and any reference sample can be used. The ability to use matched reference samples (e.g., buccal swab tissue from the same individual) is particularly important when investigating aberrations in cancer as it enables constitutional abnormalities to be filtered out.

CytoSure Haematological Cancer +SNP array

The CytoSure Haematological Cancer +SNP array (8x60k) targets regions known to be important when studying Chronic Lymphocytic Leukaemia (CLL), Multiple Myeloma (MM), Myeloproliferative Neoplasms (MPN) and Myelodysplastic Syndromes (MDS). It provides standardised, evidence-based content focusing on regions known to be important in disease progression, as well as offering whole genome ‘backbone’ coverage. In addition to accurate copy-number detection it is possible to detect LOH of regions of >30Mb.

CytoSure Cancer +SNP array

The CytoSure Cancer +SNP array (4x180k) has been designed in collaboration with Dr Jacqueline Schoumans, Head of the Cancer Cytogenetic Unit at Lausanne University Hospital and targets regions known to be important when researching disease progression for both haematological malignancies and solid tumours. In addition to offering whole genome ‘backbone’ coverage for the detection of novel aberrations, the design focuses on 1500 known cancer-associated genes which have been hand-curated from current literature. Eighteen key genes have exon-level coverage with 3-4 probes per exon enabling the detection of single exon events. The SNP probe resolution enables reporting of LOH of 20Mb.

CytoSure Consortium Cancer +SNP array

The CytoSure Consortium Cancer +SNP array (4x180k) focusses on the content recommended by the Cancer Genomics Consortium (CGC). The targeted design covers over 500 cancer genes and 130 cancer-associated genomic regions for haematological malignancies and solid tumours. The SNP probe resolution enables reporting of LOH of 10Mb. This array follows the same successful model of standardised array design and usage as introduced by ClinGen to improve the quality of clinical research.

Array	Cancer type	Copy number resolution		Loss of heterozygosity (LOH) resolution	Array format
		Backbone	Average gene resolution (Hg 19)		
CytoSure Haematological Cancer + SNP	Haematological	1 probe every 117kb	1 probe every 68kb	30Mb	8x60k
CytoSure Cancer + SNP	Haematological and solid	1 probe every 44kb	1 probe every 25kb	20Mb	4x180k
CytoSure Consortium Cancer + SNP	Haematological and solid	1 probe every 38kb	1 probe every 23kb	10Mb	4x180k

Table 1: CytoSure Cancer +SNP arrays selection guide. For a complete list of genes covered by each array, email: products@ogt.com

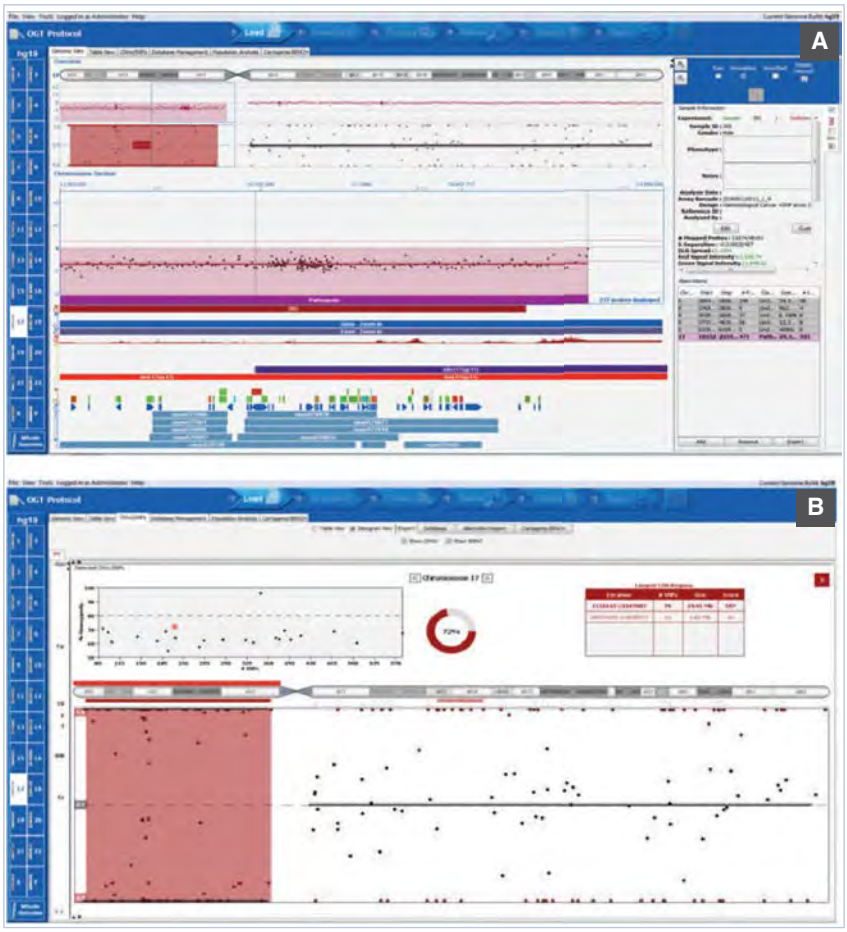


Figure 1: CytoSure Interpret Software displays both CN and SNP information. Shown here is a CLL sample run on the CytoSure Haematological Cancer +SNP Array (8x60k)*. Panel **A** shows a loss on chromosome 17 and a B-allele frequency plot summarising the SNP data. Panel **B** provides a detailed SNP analysis. CytoSure Interpret Software calculates the percentage of homozygous and heterozygous SNPs for each chromosome. Below the chromosome image, red lines indicate homozygous alleles, black heterozygous. Regions of LOH are indicated by a dark red solid rectangle and aberrations, if present, are shown above each chromosome — in this sample there is a deletion indicated by a bright red rectangle. With 72% homozygous SNPs chromosome 17 presents a clear example of a 19.9 Mb region of LOH. The size of the LOH region and the 'score' for that region is given in the table.*

* Samples kindly provided by Dr Jon Strefford, University of Southampton.

CytoSure™ products are for research use only, not for use in diagnostic procedures.

CytoSure Custom Designed aCGH Arrays

Focused custom aCGH arrays designed to your specification by the microarray experts

Custom arrays deliver:

- Complete confidence in the design of your array
- Flexible array content and format
- Customisation of any existing catalogue array
- Full custom designs including probes from our existing designs (e.g. Medical Research Exome Array), from our proprietary Oligome™ database, or new designs using our superior in-house design pipeline

High-quality aCGH arrays, perfectly matched to your exact specifications

CytoSure Custom arrays allow you to benefit from OGT's extensive array design expertise to produce an array matching your precise specifications. These arrays are ideal if you want to know the precise coordinates of an aberration by analysing specific areas of the genome at high resolution

Complete confidence in the design of your array

OGT have designed hundreds of custom arrays for some of the world's leading researchers. The array content is selected from OGT's proprietary Oligome database — a database of more than 26.5 million oligonucleotide probes, or can be *de novo* designed using the proprietry OGT probe design pipeline. All *de novo* probes are in-silico optimised and optional empirical validation of the array content ensures optimal performance. A dedicated project manager from our experienced team of bioinformaticians is assigned to each new custom design project. This gives a single point of contact throughout the process and ensures a close collaboration with our experts from initial consultation to delivery of the final design.

Flexible array content and format

CytoSure Custom arrays can be designed against any fully or partially sequenced genome as well as against sequencing data. In addition, OGT has extensively research-validated SNP content for detection of loss of heterozygosity (LOH) and uniparental disomy, which can be incorporated into the array design. CytoSure Custom arrays can be designed in a variety of formats depending on your desired level of focus, with 1, 2, 4, or 8 arrays available per slide (see Figure 1) to provide the most cost-effective solution for your research. Processing can be undertaken in your lab or in OGT's state-of-the art high-throughput laboratory in Oxford, UK.

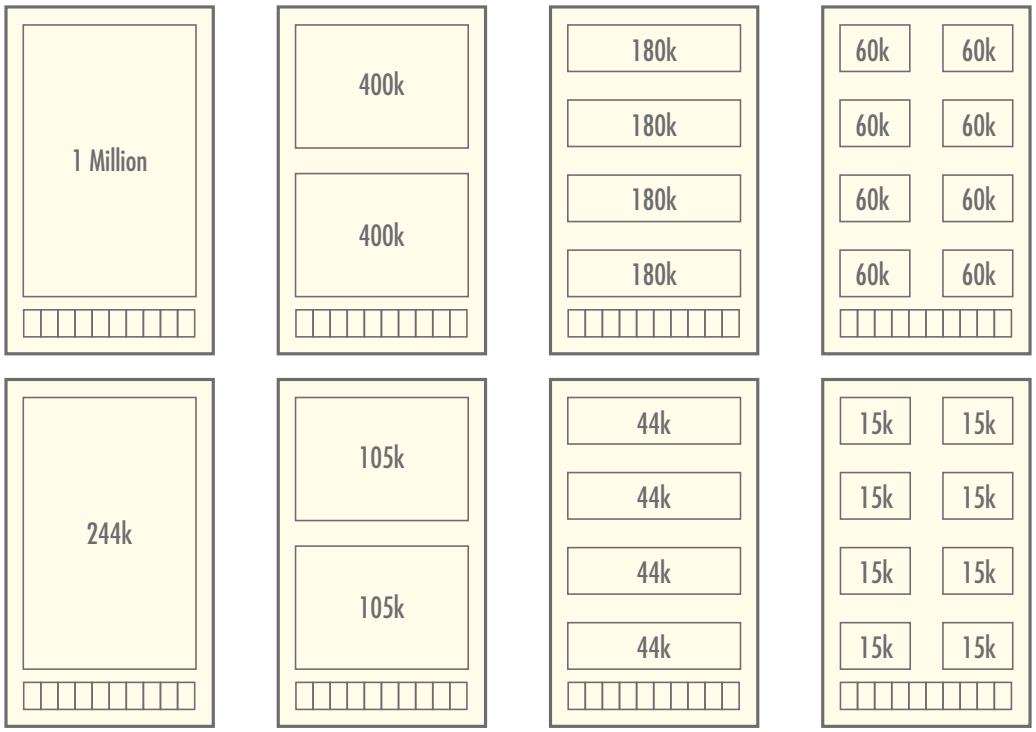


Figure 1: Multiple arrays on a single slide can reduce costs and improve efficiency.

CytoSure™ Included with all CytoSure microarrays

CytoSure Interpret Software

A powerful and easy-to-use package for analysis of aCGH data with multiple features allowing standardised data analysis (using Accelerate Workflow) or customised, user-defined analysis

CytoSure Interpret Software delivers:

- Fast, accurate and simple analysis of aCGH data
- Comprehensive data annotation with direct links to external databases and online resources
- A robust relational database allowing sophisticated data querying and filtering
- Extensive customisation options
- Fully integrated, automatic analysis of array image files

Effortless translation of oligo aCGH into meaningful results

The "Accelerate Workflow" provides automated data analysis based on predefined settings. This unique feature minimises user intervention and maximises the consistency and speed of analysis. Batch processing allows an unlimited number of samples to be analysed simultaneously with the Circular Binary Segmentation (CBS) algorithm (Figure 1). Regions of LOH are analysed with our proprietary SNP calling algorithm (Figure 2).

Direct links to external databases and online resources

CytoSure Interpret Software includes extensive annotation tracks covering syndromes, genes, exons, CNVs and segmental duplication — linked to publicly available databases such as ISCA, Decipher, Database of Genomic Variants and the Cancer Gene Census (Figure 3) providing results in context. Each track can reference hg18, hg19 or hg38 information.

Sophisticated data querying and filtering

The powerful relational database enables storage of sample data according to its relationship with other data and back-ups are straightforward with the choice of full, partial or mini back up. The database is customisable with a choice of management systems designed to integrate with your current IT infrastructure. The unique "Family Tree" viewer allows probands to be linked to other family members to view aberrations across three generations.

Designed to meet the needs of your laboratory

Complete flexibility to optimise data analysis settings and customise data reports. The permission-based log-on structure enables greater flexibility for management of user accounts.

Compatible with a variety of microarray scanners

The CytoSure Interpret Feature Extraction Module allows analysis of TIFF images from a variety of microarray scanners. The module comes pre-loaded with template files enabling images to be feature-extracted and seamlessly loaded into the Accelerate Workflow without the need for user intervention.

Figure 1: Automated aberration detection with CytoSure Interpret Software, showing clear detection of chromosomal abnormalities. The gain on chromosome 12 for this chronic lymphocytic leukaemia (CLL) sample contains the zinc finger protein gene ZP384, easily identified in the Cancer Gene Census genes track.

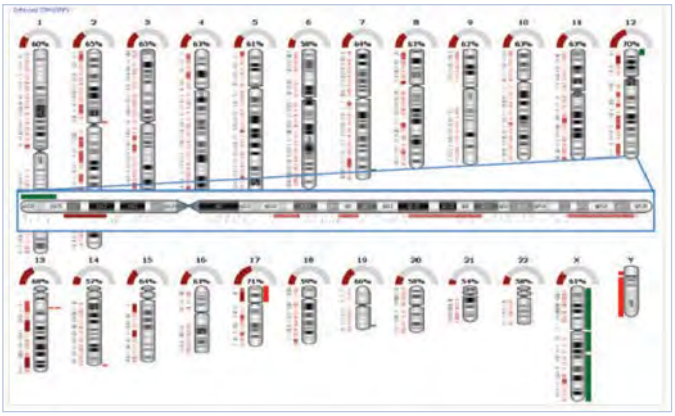


Figure 2: Automated SNP detection and LOH calling with CytoSure Interpret Software. The dark red rectangles indicate regions of LOH. The green and the bright red rectangles indicate amplifications and deletions respectively. This is the same CLL sample as displayed in Figure 1 and clearly illustrates the gain in the telomere region of the p arm and the region of LOH in p13.31-p12.3

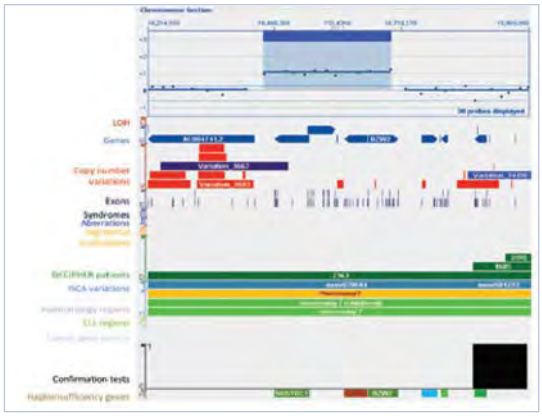


Figure 3: Fully customisable tracks simplify interpretation of aberrations.

CytoSure Genomic DNA Labelling Kits

Efficient and reproducible labelling of DNA samples for use in aCGH

CytoSure Genomic DNA Labelling Kits deliver:

- Optimised formats to suit your throughput requirements
- Reliable high-quality results through higher signal intensity
- Fast and simple procedure

Everything you need, from reagents to plasticware

The labelling of DNA samples used in aCGH (array comparative genomic hybridisation) is a critical step in the experimental process as poor labelling can result in inaccurate data. As part of a complete labelling solution — protocols, reagents, clean-up plates or columns and collection tubes — OGT's CytoSure Genomic DNA Labelling Kits have been uniquely developed and optimised to enable rapid delivery of high-quality results with high signal-to-noise ratios.

Tested with a wide range of sample types to ensure optimal performance

Offering reliable, high-quality results, the CytoSure Genomic DNA Labelling Kits ensure superior signal-to-noise ratios for confident detection of copy number variation. This high signal-to-noise ratio means that even small aberrations can be reliably detected (Figure 1).

CytoSure Genomic DNA Labelling Kits offer much faster DNA labelling and clean up than traditional enzymatic labelling procedures. Labelling reactions using both the 24 and 96 reaction kits can easily be completed in a single day (Figure 2). The procedure can also be automated for implementation in high-throughput workflows.

Product	Contents	Cat. No.
CytoSure Genomic DNA Labelling Kit	24 reactions: clean-up columns, dyes, nucleotide mix, random primers, enzyme, collection tubes	020020
CytoSure HT Genomic DNA Labelling Kit	96 reactions: 2 purification plates, nucleotide mix, random primers, enzyme	500040

Figure 1: Reliable detection of small aberrations. DNA labelled using the CytoSure Genomic DNA Labelling Kit was run on a CytoSure ISCA 8x60K array. CytoSure Interpret Software combined with high DNA signal intensity allowed detection of a small (130 kb) DNA amplification.

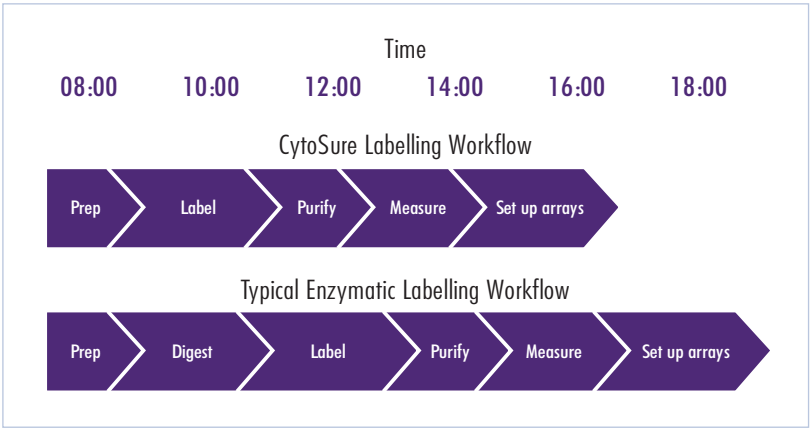


Figure 2: Two typical labelling workflows: With no need to digest, CytoSure Genomic DNA Labelling Kits save you at least 2 hours.

CytoSure™

CytoSure Spikes A-D: Cat. No. **500068** (12 assays of each)

CytoSure Spikes A-H: Cat. No. **500066** (12 assays of each)

CytoSure Sample Tracking Spike-ins

Reliable sample identity tracking for use with CytoSure arrays

CytoSure Sample Tracking Spike-ins deliver:

- Confidence in results
- Simple one-step procedure with no alteration to existing workflows
- Easy identification of sample mix-up

Complete confidence in results

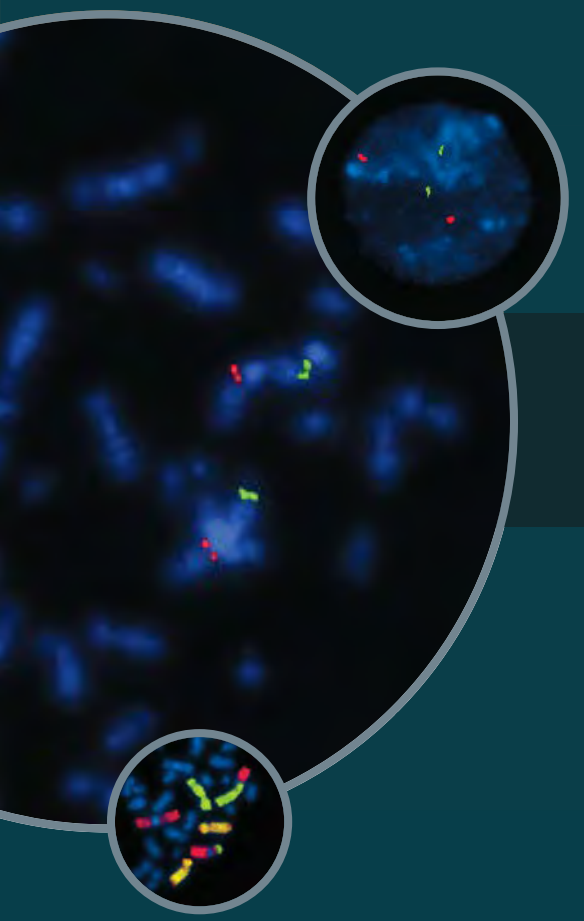
Increasing numbers of aCGH (array comparative genomic hybridisation) samples combined with higher-throughput array formats means that it is imperative to track samples throughout the labelling, hybridisation and analysis process to maintain sample identity. CytoSure Sample Tracking Spike-ins are uniquely designed to enable reliable sample tracking and easy identification of sample mix-up using OGT's class-leading CytoSure Arrays and CytoSure Interpret Software.

Each CytoSure Sample Tracking Spike-in is designed to a specific, unique region of the genome. Oligonucleotide probes complementary to the sample tracking spike-ins are included on all of the arrays supplied and optimised by Oxford Gene Technology (OGT). Eight different CytoSure Sample Tracking Spike-ins are available. Each spike-in has been carefully prepared to ensure that there is no cross-hybridisation with other probes on the array or with any other region on the genome. In addition, colour-coded caps are used for ease of identification, aiding correct usage.

Accessories

Product	Description	Cat. No.
Oligo aCGH/ChIP-on-Chip Hybridization Kit	Hybridisation reagents for 100 samples	500013
	Hybridisation reagents for 25 samples	500014
DNA clean up plate	96 well plate for the clean up of DNA	500041
DNA clean up columns	24 columns for the clean up of DNA	500020
Wash Buffer 1 & 2 set	Buffers for post hybridisation washing of arrays – 3 x 4L	500015
Backing slides (gaskets)	Backing slides for 8 x arrays	500010
	Backing slides for 4 x arrays	500011
	Backing slides for 2 x arrays	500012
	Backing slides for 1 x arrays	500017
COT Human DNA (250µl)	Blocking reagent to prevent non-specific hybridisation	500025
Human Genomic DNA, Male (100µg)	Reference DNA	500026
Human Genomic DNA, Female (100µg)	Reference DNA	500027

Cytocell
an OGT company
aquarius



Indices of FISH probes

Cytocell
an OGT company

Aquarius® Haematology Probe Range Summary

Probe Name	Chromosome Region	Probe Type	Control Probe	No. Tests	Cat. No.*
13q14.3	13q14.2-q14.3	Deletion	D13S1825	5 or 10	LPH 006
Alpha Satellite 12 *Plus* for CLL	12p11.1-q11.1	Enumeration	–	5 or 10	LPH 069
AML1 (RUNX1)	21q22.12	Breakapart	–	5 or 10	LPH 027
AML1/ETO (RUNX1/RUNX1T1) Dual Fusion	21q22.12/8q21.3	Translocation	–	5 or 10	LPH 026
ATM	11q22.3	Deletion	D11Z1	5 or 10	LPH 011
BCL6	3q27.3	Breakapart	–	5 or 10	LPH 035
BCR/ABL (ABL1) Dual Fusion	22q11.22-q11.23/9q34.11-q34.12	Translocation	–	5 or 10	LPH 007
BCR/ABL (ABL1) *Plus* Dual Fusion	22q11.22-q11.23/9q34.11-q34.12	Translocation	–	5 or 10	LPH 038
CBFβ /MYH11 Dual Fusion	16p13.11/16q22.1	Translocation	–	5 or 10	LPH 022
CKS1B/CDKN2C (P18)	1p32.3/1q21.3	Amplification/Deletion	–	5 or 10	LPH 039
cMYC (MYC)	8q24.21	Breakapart	–	5 or 10	LPH 010
CRLF2	Xp22.33/Yp11.32	Breakapart	–	50µl or 100µl	RU-LPH 085**
D13S319 *Plus*	13q14.2-q14.3	Deletion	LAMP1	5 or 10	LPH 068
D13S319/13qter/12cen	13q14.2-q14.3/12p11.1-q11.1	Deletion/Enumeration	LAMP1	5 or 10	LPH 066
D13S25	13q14.3	Deletion	D13S1825	5 or 10	LPH 043
Del(5q)	5p15.31-5q13.2	Deletion	5p15.31	5 or 10	LPH 024
Del(7q)	7q22.1-q22.2/7q31.2	Deletion	–	5 or 10	LPH 025
Del(20q)	20q12/20q13.12	Deletion	–	5 or 10	LPH 020
E2A (TCF3)	19p13.3	Breakapart	–	5 or 10	LPH 019
E2A (TCF3)/PBX1 Dual Fusion	19p13.3/1q23.3	Translocation	–	5 or 10	LPH 079
E2A (TCF3)/PBX1/HLF Dual Fusion	19p13.3/1q23.3/17q22	Translocation	–	5 or 10	LPH 080
EVI1 (MECOM)	3q26.2	Breakapart	–	5 or 10	LPH 036
FIP1L1/CHIC2/PDGFRA	4q12	Deletion/Fusion	–	5 or 10	LPH 032
IGH	14q32.33	Breakapart	–	5 or 10	LPH 014
IGH *Plus*	14q32.33	Breakapart	–	5 or 10	LPH 070
IGH/BCL2 *Plus* Dual Fusion	14q32.33/18q21.33	Translocation	–	5 or 10	LPH 071
IGH/CCND1 *Plus* Dual Fusion	14q32.33/11q13.3	Translocation	–	5 or 10	LPH 072
IGH/CCND3 *Plus* Dual Fusion	14q32.33/6p21	Translocation	–	5 or 10	LPH 075
IGH/cMYC (MYC) *Plus* Dual Fusion	14q32.33/8q24.21	Translocation	–	5 or 10	LPH 076
IGH/FGFR3 *Plus* Dual Fusion	14q32.33/4p16.3	Translocation	–	5 or 10	LPH 074
IGH/MAF *Plus* Dual Fusion	14q32.33/16q23.1-q23.2	Translocation	–	5 or 10	LPH 073
IGH/MAFB *Plus* Dual Fusion	14q32.33/20q12	Translocation	–	5 or 10	LPH 077
IGH/MYEOV *Plus* Dual Fusion	14q32.33/11q13.3	Translocation	–	5 or 10	LPH 078
IGK	2p11.2	Breakapart	–	5 or 10	LPH 034
IGL	22q11.21-q11.23	Breakapart	–	5 or 10	LPH 033
MLL (KMT2A)	11q23.3	Breakapart	–	5 or 10	LPH 013
MLL/AFF1 Dual Fusion	11q23.3/4q21.3-q22.1	Translocation	–	5 or 10	LPH 081
MLL/MLLT1 Dual Fusion	11q23.3/19p13.3	Translocation	–	50µl or 100µl	RU-LPH 082**
MLL/MLLT3 Dual Fusion	11q23.3/9p21.3	Translocation	–	50µl or 100µl	RU-LPH 083**
MLL/MLLT4 Dual Fusion	11q23.3/6q27	Translocation	–	50µl or 100µl	RU-LPH 084**
MYB	6q23.3	Deletion	D6Z1	5 or 10	LPH 016
P16 (CDKN2A)	9p21.3	Deletion	D9Z3	5 or 10	LPH 009
P2RY8	Xp22.33/Yp11.32	Deletion	–	50µl or 100µl	RU-LPH 086**
P53 (TP53)	17p13.1	Deletion	D17Z1	5 or 10	LPH 017
P53 (TP53)/ATM Probe Combination	17p13.1/11q22.3	Deletion	–	5 or 10	LPH 052
PDGFRB	5q32	Breakapart	–	5 or 10	LPH 031
FAST PML/RARα (RARA) Dual Fusion	15q24.1/17q21.1-q21.2	Translocation	–	5 or 10	LPH 064
PML/RARα (RARA) Dual Fusion	15q24.1/17q21.1-q21.2	Translocation	–	5 or 10	LPH 023
RARα (RARA)	17q21.1-q21.2	Breakapart	–	5 or 10	LPH 065
TCL1	14q32.13-q32.2	Breakapart	–	5 or 10	LPH 046
TCRAD	14q11.2	Breakapart	–	5 or 10	LPH 047
TCRB (TRB)	7q34	Breakapart	–	5 or 10	LPH 048
TEL/AML1 (ETV6/RUNX1) Dual Fusion	12p13.2/21q22.12	Translocation	–	5 or 10	LPH 012
TLX1	10q24.31	Breakapart	–	5 or 10	LPH 049
TLX3	5q35.1	Breakapart	–	5 or 10	LPH 050

* For 5 test kit add -S to catalogue number, e.g: LPH ###-S

** For research use only, not for use in diagnostic procedures.

CLL PROFILER Kit, LPH 067*

Product Description	Chromosome Region	Probe Type	Control Probe	No. Tests
P53 (TP53)/ATM	17p13.1/11q22.3	Deletion	–	5 or 10
D13S319/13qter/12cen	13q14.2-14.3/12p11.1-q11.1	Deletion/Enumeration	LAMP1	5 or 10

* For 5 test kit add -S to catalogue number, e.g: LPH ###-S

CLL *Plus* Screening Panel, LPH 087*

Product Description	Chromosome Region	Probe Type	Control Probe	No. Tests
P53 (TP53)	17p13	Deletion	D17Z1	5 or 10
ATM	11q22.3	Deletion	D11Z1	5 or 10
MYB	6q23	Deletion	D6Z1	5 or 10
13q14.3	13q14.3	Deletion	D13S1825	5 or 10
Alpha Satellite 12 *Plus* for CLL	12p11.1-q11.1	Enumeration	–	5 or 10

* For 5 test kit add -S to catalogue number, e.g: LPH ###-S

Chromoprobe Multiprobe® - ALL v2 System Range Summary

Probe Name	No. of Devices	Cat. No.
Chromoprobe Multiprobe® - ALL v2	2	PMP 030
Chromoprobe Multiprobe® - ALL v2	5	PMP 031
Chromoprobe Multiprobe® - ALL v2	10	PMP 032
Chromoprobe Multiprobe® - ALL v2	20	PMP 033*

* Supplied as 4 x 5 Multiprobe devices

Chromoprobe Multiprobe® - CLL System Range Summary

Probe Name	No. of Devices	Cat. No.
Chromoprobe Multiprobe® - CLL	2	PMP 018
Chromoprobe Multiprobe® - CLL	5	PMP 017
Chromoprobe Multiprobe® - CLL	10	PMP 016
Chromoprobe Multiprobe® - CLL	20	PMP 020*

* Supplied as 4 x 5 Multiprobe devices

Chromoprobe Multiprobe® - AML/MDS System Range Summary

Probe Name	No. of Devices	Cat. No.
Chromoprobe Multiprobe® - AML/MDS	2	PMP 025
Chromoprobe Multiprobe® - AML/MDS	5	PMP 026
Chromoprobe Multiprobe® - AML/MDS	10	PMP 027
Chromoprobe Multiprobe® - AML/MDS	20	PMP 028*

* Supplied as 4 x 5 Multiprobe devices

Cytocell
an OGT company

Aquarius® Tissue Pretreatment Kit Summary

Product Description	Kit Format	Cat. No.
Aquarius® Tissue Pretreatment Kit*	Reagent 1 (1x1l), Reagent 2 (1x10ml)	LPS 100

* This product is provided under an agreement between Life Technologies Corporation and Cytocell Ltd and is available for human diagnostic or life science use only.

Aquarius® Haematopathology Probe Range Summary

Probe Name	Chromosome Region	Probe Type	Control Probe	No. Tests	Cat. No.*
BCL2	18q21.33-q22.1	Breakapart	–	5 or 10	LPS 028
BCL6	3q27.3-q28	Breakapart	–	5 or 10	LPS 029
CCND1	11q13.3	Breakapart	–	5 or 10	LPS 030
IGH	14q32.33	Breakapart	–	5 or 10	LPS 032
IGH/BCL2 Dual Fusion	14q32.33/18q21.33	Translocation	–	5 or 10	LPS 033
IGH/CCND1 Dual Fusion	14q32.33/11q13.3	Translocation	–	5 or 10	LPS 031
IGH/MALT1 Dual Fusion	14q32.33/18q21.31-q21.32	Translocation	–	5 or 10	LPS 034
IGH/MYC Dual Fusion	14q32.33/8q24.21	Translocation	–	5 or 10	LPS 035
IGK	2p11.2	Breakapart	–	5 or 10	LPS 038
IGL	22q11.21-q11.23	Breakapart	–	5 or 10	LPS 039
MALT1	18q21.31-q21.32	Breakapart	–	5 or 10	LPS 017
MYC	8q24.21	Breakapart	–	5 or 10	LPS 027
P16 (CDKN2A)	9p21.3	Deletion	D9Z3	5 or 10	LPS 036
P53 (TP53)	17p13.1	Deletion	D17Z1	5 or 10	LPS 037
RB1	13q14.2	Deletion	LAMP1	5 or 10	LPS 011

* For 5 test kit add -S to catalogue number, e.g: LPS ###-S

Aquarius® Pathology Probe Range Summary

Probe Name	Chromosome Region	Probe Type	Control Probe	No. Tests	Cat. No.*
1p36/1q25 and 19q13/19p13 Kit	1p36.32/19q13.33	Deletion	1q25.2/19p13.2	5 or 10	LPS 047
ALK	2p23.2-p23.1	Breakapart	–	5 or 10	LPS 019
CHOP (DDIT3)	12q13.3	Breakapart	–	5 or 10	LPS 015
C-MET (MET)	7q31.2	Amplification	D7Z1	5 or 10	LPS 004
EGFR	7p11.2	Amplification	D7Z1	5 or 10	LPS 003
EML4	2p21	Breakapart	–	5 or 10	LPS 020
EWSR1	22q12.1-q12.2	Breakapart	–	5 or 10	LPS 006
EWSR1/ERG Dual Fusion	21q22.13-q22.2/22q12.1-q12.2	Translocation	–	5 or 10	LPS 008
FGFR1	8p11.23-p11.22	Breakapart/Amplification	D8Z2	5 or 10	LPS 018
FLI1/EWSR1 Dual Fusion	11q24.3/22q12.1-q12.2	Translocation	–	5 or 10	LPS 007
HER2 (ERBB2)	17q12	Amplification	D17Z1	5 or 10	LPS 001
MDM2	12q15	Amplification	D12Z1	5 or 10	LPS 016
N-MYC (MYCN)	2p24.3/2q11.2	Amplification	AFF3	5 or 10	LPS 009
PAX3	2p36.1	Breakapart	–	5 or 10	LPS 012
PAX7	1p36.13	Breakapart	–	5 or 10	LPS 013
ROS1	6q22.1	Breakapart	–	5 or 10	LPS 022
SRD (CHD5)	1p36.31	Deletion	ZNF672	5 or 10	LPS 010
SYT (SS18)	18q11.2	Breakapart	–	5 or 10	LPS 014
TMPRSS2/ERG	21q22.2-q22.3/21q22.13-q22.2	Deletion/Breakapart	ERG	5 or 10	LPS 021
TOP2A	17q21.2	Amplification/Deletion	D17Z1	5 or 10	LPS 002
ZNF217	20q13.2	Amplification	DEFB128	5 or 10	LPS 005

* For 5 test kit add -S to catalogue number, e.g: LPS ###-S

Aquarius® *FAST* FISH Prenatal Probe Range Summary

Product Description	Locus	Chromosome Region	No. Tests	Cat. No.*
Probe Set 1 and 2			5, 10, 30 or 50	LPF 001
X centromere	DXZ1	Xp11.1-q11.1		
Y centromere	DYZ3	Yp11.1-q11.1		
18 centromere	D18Z1	18p11.1-q11.1		
13 unique sequence	N/A	13q14.2		
21 unique sequence	N/A	21q22.13		
Probe Set 1			5 or 10	LPF 002
X centromere	DXZ1	Xp11.1-q11.1		
Y centromere	DYZ3	Yp11.1-q11.1		
18 centromere	D18Z1	18p11.1-q11.1		
Probe Set 2			5 or 10	LPF 003
13 unique sequence	N/A	13q14.2		
21 unique sequence	N/A	21q22.13		

* For 5, 30 or 50 test kit add -S, -30 or -50 to the catalogue number respectively, e.g: LPF### -S, LPF### -30 or LPF### -50

Aquarius® Prenatal Probe Range Summary

Product Description	Locus	Chromosome Region	No. Tests	Cat. No.*
Probe Set 1 and 2			5, 10, 30 or 50	LPA 001
X centromere	DXZ1	Xp11.1-q11.1		
Y centromere	DYZ3	Yp11.1-q11.1		
18 centromere	D18Z1	18p11.1-q11.1		
13 unique sequence	N/A	13q14.2		
21 unique sequence	N/A	21q22.13		
Probe Set 1			5 or 10	LPA 002
X centromere	DXZ1	Xp11.1-q11.1		
Y centromere	DYZ3	Yp11.1-q11.1		
18 centromere	D18Z1	18p11.1-q11.1		
Probe Set 2			5 or 10	LPA 003
13 unique sequence	N/A	13q14.2		
21 unique sequence	N/A	21q22.13		
Probe Set 3			5 or 10	LPA 005
13 unique sequence	N/A	13q14.2		
18 centromere	D18Z1	18p11.1-q11.1		
21 unique sequence	N/A	21q22.13		
18 centromere blue	D18Z1	18p11.1-q11.1	5 or 10	LPA 004

* For 5, 30 or 50 test kit add -S, -30 or -50 to the catalogue number respectively, e.g: LPA### -S, LPA### -30 or LPA### -50

Cytocell
an OGT company

Aquarius® Microdeletion Probe Range Summary

Probe Name	Chromosome Region	Probe Loci	Control Probe	No. Tests	Cat. No.*
Alagille (JAG1)	20p12.2	JAG1	20qter	5 or 10	LPU 012
Angelman (UBE3A/D15S10)	15q11.13	UBE3A/D15S10	15qter	5 or 10	LPU 006
CHARGE	8q12.1-q12.2	CHD7	D8Z2	5 or 10	LPU 021
Cri-Du-Chat and Sotos Probe Combination	5p15.31/5p15.2/5q35	UBE2QL1, CTNND2, NSD1	–	5 or 10	LPU 013
DiGeorge II (10p14)	10p14	CELF2	D10Z1	5 or 10	LPU 015
DiGeorge TBX1 and 22q13.3 Probe Combination	22q11.21/22q13.33	TBX1, SHANK3	–	5 or 10	LPU 014
DiGeorge/VCFS N25 and 22q13.3 Probe Combination	22q11.21/22q13.33	N25/D22S75, SHANK3	–	5 or 10	LPU 010
DiGeorge/VCFS TUPLE1 and 22q13.3 Probe Combination	22q11.21/22q13.33	TUPLE1, SHANK3	–	5 or 10	LPU 004
Kallmann (KAL1) and Steroid Sulphatase Deficiency (STS) Probe Combination	Xp22.31	KAL1, STS	DXZ1	5 or 10	LPU 016
Langer-Giedion	8q23.3/8q24.11	TRPS1, EXT1	D8Z2	5 or 10	LPU 022
Monosomy 1p36	1p36.33	SKI	1qter	5 or 10	LPU 020
Neurofibromatosis Type 1	17q11.2	NF1	17pter	5 or 10	LPU 017
Prader-Willi/Angelman (SNRPN)	15q11.2	SNRPN	15qter	5 or 10	LPU 005
Rubinstein-Taybi	16p13.3	CREBBP	D16Z2	5 or 10	LPU 023
Saethre-Chotzen/Williams-Beuren Probe Combination	7p21.1/7q11.23	TWIST1, WBSCR/ELN	–	5 or 10	LPU 024
SHOX	Xp22.33/Yp11.32	SHOX	DXZ1, DYZ1	5 or 10	LPU 025
Smith-Magenis (RAI1)/ Miller-Dieker Probe Combination	17p11.2/17p13.3	RAI1, PAFAH1B1	–	5 or 10	LPU 019
Smith-Magenis (FLII)/ Miller-Dieker Probe Combination	17p11.2/17p13.3	FLII, PAFAH1B1	–	5 or 10	LPU 007
SRY	Yp11.31	SRY	DXZ1, DYZ1	5 or 10	LPU 026
Williams-Beuren	7q11.23	WBSCR/ELN	D7Z1	5 or 10	LPU 011
Wolf-Hirschhorn	4p16.3	MMSET, NEFLA	4qter	5 or 10	LPU 009
XIST	Xq13.2	XIST	DXZ1	5 or 10	LPU 018

* For 5 test kit add -S to catalogue number, e.g: LPU ###-S

Aquarius® Whole Chromosome Painting Probe Range Summary

Chromosome	Fluorescent Label	No. Tests	Cat. No.*
1	Red or Green	5	LPP 01R/G
2	Red or Green	5	LPP 02R/G
3	Red or Green	5	LPP 03R/G
4	Red or Green	5	LPP 04R/G
5	Red or Green	5	LPP 05R/G
6	Red or Green	5	LPP 06R/G
7	Red or Green	5	LPP 07R/G
8	Red or Green	5	LPP 08R/G
9	Red or Green	5	LPP 09R/G
10	Red or Green	5	LPP 10R/G
11	Red or Green	5	LPP 11R/G
12	Red or Green	5	LPP 12R/G
13	Red or Green	5	LPP 13R/G
14	Red or Green	5	LPP 14R/G
15	Red or Green	5	LPP 15R/G
16	Red or Green	5	LPP 16R/G
17	Red or Green	5	LPP 17R/G
18	Red or Green	5	LPP 18R/G
19	Red or Green	5	LPP 19R/G
20	Red or Green	5	LPP 20R/G
21	Red or Green	5	LPP 21R/G
22	Red or Green	5	LPP 22R/G
X	Red or Green	5	LPP 0XR/G
Y	Red or Green	5	LPP 0YR/G

* R specifies a red label, G specifies a green label

Whole Chromosome Paint Combinations

Chromosome	Description	No. Tests	Cat. No.*
1/2/4	Whole chromosome paint combination 1,2,4 (3 colour, 3 probe combination) directly labelled	10	LPP 124

* Minimum order of ten units (100 tests). Orders are subject to 4-6 weeks lead time

Chromoprobe Multiprobe®-OctoChrome™ Paint System Range Summary

Probe Name	No. of Devices	Cat. No.
Chromoprobe Multiprobe® - OctoChrome™ System	2	PMP 802
Chromoprobe Multiprobe® - OctoChrome™ System	5	PMP 804
Chromoprobe Multiprobe® - OctoChrome™ System	10	PMP 803

Cytocell
an OGT company

Aquarius® Satellite Enumeration Probe Range Summary

Chromosome	Locus	Chromosome Region	DNA Class	No. Tests	Cat. No.*
1	D1Z1	1q12	satellite III	5	LPE 001R/G
2	D2Z2	2p11.1-q11.1	α-satellite	5	LPE 002R/G
3	D3Z1	3p11.1-q11.1	α-satellite	5	LPE 003R/G
4	D4Z1	4p11.1-q11.1	α-satellite	5	LPE 004R/G
1/5/19	D1Z7 D5Z2 D19Z3	1p11.1-q11.1 5p11.1-q11.1 19p11.1-q11.1	α-satellite	5	LPE 005R/G
6	D6Z1	6p11.1-q11.1	α-satellite	5	LPE 006R/G
7	D7Z1	7p11.1-q11.1	α-satellite	5	LPE 007R/G
8	D8Z2	8p11.1-q11.1	α-satellite	5	LPE 008R/G
	D8Z2	8p11.1-q11.1	α-satellite	10	LPE 008B
9	D9Z3	9q12	satellite III	5	LPE 009R/G
10	D10Z1	10p11.1-q11.1	α-satellite	5	LPE 010R/G
11	D11Z1	11p11.1-q11.1	α-satellite	5	LPE 011R/G
12	D12Z3 D12Z3	12p11.1-q11.1 12p11.1-q11.1	α-satellite α-satellite	5 10	LPE 012R/G LPE 012B
13/21	D13Z1 D21Z1	13p11.1-q11.1 21p11.1-q11.1	α-satellite	5	LPE 013R/G
14/22	D14Z1 D22Z1	14p11.1-q11.1 22p11.1-q11.1	α-satellite	5	LPE 014R/G
15	D15Z4	15p11.1-q11.1	α-satellite	5	LPE 015R/G
16	D16Z2	16p11.1-q11.1	α-satellite	5	LPE 016R/G
17	D17Z1 D17Z1	17p11.1-q11.1 17p11.1-q11.1	α-satellite α-satellite	5 10	LPE 017R/G LPE 017RB
18	D18Z1	18p11.1-q11.1	α-satellite	5	LPE 018R/G
20	D20Z1	20p11.1-q11.1	α-satellite	5	LPE 020R/G
X	DXZ1	Xp11.1-q11.1	α-satellite	5	LPE 0XR/G
Yc	DYZ3	Yp11.1-q11.1	α-satellite	5	LPE 0YcR/G
Yq	DYZ1	Yq12	satellite III	5	LPE 0YqR/G
XYc Dual Labelled	DXZ1 DYZ3	Xp11.1-q11.1 Yp11.1-q11.1	α-satellite	10	LPE 0XYc
XYq Dual Labelled	DXZ1 DYZ1	Xp11.1-q11.1 Yq12	α-satellite satellite III	10	LPE 0XYq

* R specifies a red label, G specifies a green label and B specifies a blue label.

Acro-P-Arm Probe

Chromosome	Colour	No. Tests	Cat. No.
13, 14, 15, 21, 22	Red	10	LPE NOR

Aquarius® Subtelomere Specific Probe Range Summary

Probe Specificity	Clone Name	Marker (STS)	Max. physical distance from Telomere (kb)	Cat. No.*
1p	CEB108	RH120573	987	LPT 01PR/G
1q	160H23	GDB:315525	54	LPT 01QR/G
2p	dJ892G20	D2S2983	18	LPT 02PR/G
2q	dJ1011O17	D2S2986	277	LPT 02QR/G
2q NP	172I13	D2S447	311	LPT 02QNPR/G
3p	dJ1186B18	D3S4559	213	LPT 03PR/G
3q	196F4	D3S1272	959	LPT 03QR/G
4p	36P21	D4S3360	67	LPT 04PR/G
4q	dJ963K6	D4S139	372	LPT 04QR/G
5p	189N21	RH120167	2254	LPT 05PR/G
5q	240G13	D5S2907	222	LPT 05QR/G
6p	62I11	STS-H99640	147	LPT 06PR/G
6q	57H24	D6S2522	230	LPT 06QR/G
7p	109a6	RH104000	118	LPT 07PR/G
7q	2000a5	RH48601	138	LPT 07QR/G
8p	dJ580L5	RH40619	150	LPT 08PR/G
8q	489D14	D8S595	202	LPT 08QR/G
9p	43N6	RH65569	226	LPT 09PR/G
9q	112N13	D9S2168	167	LPT 09QR/G
10p	306F7	STS-N35887	271	LPT 10PR/G
10q	137E24	RH44494	138	LPT 10QR/G
11p	dJ908H22	D11S2071	189	LPT 11PR/G
11q	dJ770G7	D11S4974	3447	LPT 11QR/G
12p	496A11	D12S200	771	LPT 12PR/G
12q	221K18	RH81094	90	LPT 12QR/G
13q	163C9	D13S1825	17	LPT 13QR/G
14q	dJ820M16	D14S1420	143	LPT 14QR/G
15q	154P1	D15S936	328	LPT 15QR/G
16p	121I4	SHGC-16929	147	LPT 16PR/G
16q	240G10	RH80305	331	LPT 16QR/G
17p	2111b1	D17S2199	143	LPT 17PR/G
17q	362K4	–	34	LPT 17QR/G
18p	74G18	D18S552	141	LPT 18PR/G
18q	dJ964M9	D18S1390	155	LPT 18QR/G
19p	dJ546C11	D19S676E	260	LPT 19PR/G
19q	F21283	RH102404	49	LPT 19QR/G
20p	dj1061L1	D20S210	165	LPT 20PR/G
20q	81F12	RH10656	153	LPT 20QR/G
21q	63H24	D21S1446	29	LPT 21QR/G
22q	99K24	D22S1726	101	LPT 22QR/G
XpYp**	839D20	DXYS129	344	LPT XYPR/G
XqYq***	225F6	DXYS154	64	LPT XYQR/G
	C8.2/1	SYBL1	131	LPT XYQR/G

* R specifies a red label, G specifies a green label
** This probe is specific for the p-arms of both X and Y
*** This probe is specific for the q-arms of both X and Y
NP Non Polymorphic

Cytocell
an OGT company

Telomark

Probe Specificity	Marker (STS)	Max. physical distance from Telomere (kb)	Notes and Source	Cat. No.*
1p	SHGC-74122	848	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK01
1q	GDB:315525	54	TelomereA6 / CTB-160H23 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK01
2p	D2S2983	18	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK02
2q NP	D2S447	311	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK02
3p	D3S4559	213	TelomereA3 / PAC1186B18 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK03
3q	RH12742	388	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK03
4p	D4S3360	67	TelomereA5 / CTC-36P21 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK04
4q	D4S139	371	Sequenced - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK04
5p	D5S1680E	372	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK05
5q	D5S2907	222	TelomereA7 / CTC-240G13 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK05
6p	STS-H99640	147	TelomereA8 / CTB-62l11 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK06
6q	D6S2522	230	TelomereA9 / CTB-57H24 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK06
7p	RH104000	118	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK07
7q	RH48601	138	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK07
8p	D8S1482	407	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK08
8q	D8S595	202	TelomereA12 / CTC-489D14 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK08
9p	RH65569	226	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK09
9q	D9S1090	385	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK09
10p	STS-N35887	271	TelomereB1 / CTC-306F7 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK10
10q	RH102433	108	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK10
11p	D11S2071	189	TelomereB3 / CTC-908H22 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK11
11q	D11S1110	764	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK11
12p	D12S200	771	TelomereB5 / CTC-496A11 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK12
12q	RH81094	90	TelomereB6 / CTC-221K18 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK12
13q	D13S1825	17	Sequenced - UCSC hg38 (2013)	LPT MRK/LPT MRK06
14q	D14S1420	143	TelomereB8 / CTC-820M16 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK07
15q	D15S936	328	TelomereB9 / CTB-154P1 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK10
16p	SHGC-16929(UCSC)	147	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK13
16q	RH80305	331	TelomereB11 / CTC-240G10 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK13
17p	D17S2199	143	Sequenced - UCSC hg38 (2013)	LPT MRK/LPT MRK08
17q	SHGC-144868	399	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK09
18p	D18S552	141	TelomereG9 / GS1-74G18 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK11
18q	D18S1390	155	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK12
19p	D19S676E	260	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK14
19q	RH102404	49	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK14
19q	D19S829	178	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK14
20p	D20S210	165	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK15
20q	RH10656	153	Sequenced - UCSC hg38 (2013)	LPT MRK/LPT MRK15
21q	D21S1446	29	TelomereC3 / CTB-63H24 - Ensembl Ver.75 (2014)	LPT MRK/LPT MRK04
22q	D22S1726	101	Sequenced - Ensembl Ver.55 (2009)	LPT MRK/LPT MRK03
XpYp	DXYS129	288	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK01
XpYp	DXYS129	331	Ensembl Ver.74 (GRCh37) 2013	LPT MRK/LPT MRK01
XqYq	DXYS154	64	Flanking PCR est. - Ensembl Ver.74 (2013)	LPT MRK/LPT MRK02

* For 5 test kit add -S to catalogue number, e.g: LPS MRK ##-S

Chromoprobe Multiprobe®-T Subtelomere System Range Summary

Probe Name	No. of Devices	Cat. No.
Chromoprobe Multiprobe® - T System	2	PMP 009
Chromoprobe Multiprobe® - T System	5	PMP 008
Chromoprobe Multiprobe® - T System	10	PMP 007

Aquarius® Murine Painting Probe Range Summary

Chromosome	Fluorescent Label	No. Tests	Cat. No.*
1	Red or Green	5 or 10	AMP 01R/G
2	Red or Green	5 or 10	AMP 02R/G
3	Red or Green	5 or 10	AMP 03R/G
4	Red or Green	5 or 10	AMP 04R/G
5	Red or Green	5 or 10	AMP 05R/G
6	Red or Green	5 or 10	AMP 06R/G
7	Red or Green	5 or 10	AMP 07R/G
8	Red or Green	5 or 10	AMP 08R/G
9	Red or Green	5 or 10	AMP 09R/G
10	Red or Green	5 or 10	AMP 10R/G
11	Red or Green	5 or 10	AMP 11R/G
12	Red or Green	5 or 10	AMP 12R/G
13	Red or Green	5 or 10	AMP 13R/G
14	Red or Green	5 or 10	AMP 14R/G
15	Red or Green	5 or 10	AMP 15R/G
16	Red or Green	5 or 10	AMP 16R/G
17	Red or Green	5 or 10	AMP 17R/G
18	Red or Green	5 or 10	AMP 18R/G
19	Red or Green	5 or 10	AMP 19R/G
X	Red or Green	5 or 10	AMP 0XR/G
Y	Red or Green	5 or 10	AMP 0YR/G

* R specifies a red label and G specifies a green label.

* For 5 test kit add -S to catalogue number, e.g: AMP ###-S

Accessories

Cat. No.	Description	Unit Size
PCN004	Hybridisation Chamber	1
PCN007	24 Square Template Slides	100
PCN008	8 Square Template Slides	100
PCN002	Cytocell Slide Surface Thermometer	4

Ancillary Reagents

Cat. No.	Description	Unit Size
PCA005	Rubber Solution Glue	15g
PCN003	Mounting Medium	10ml
DES500L	0.125µg/ml DAPI	500µl
DES1000L	0.125µg/ml DAPI	1000µl
DFS500L	1.0µg/ml DAPI	500µl
DSS500L	0.0625µg/ml DAPI	500µl
HA500L	Hybridisation Solution A	500µl
HA1000L	Hybridisation Solution A	1000µl
HB500L	Hybridisation Solution B	500µl
HB1000L	Hybridisation Solution B	1000µl
PCA003	20x SSC	100ml

Microscope Filters*

Cat. No.	Description	Unit Size
N/A	FITC Filter	1
N/A	DAPI Filter	1
N/A	Texas Red Filter	1
N/A	DEAC Filter	1
N/A	FITC/Texas Red Dual Filter	1
N/A	FITC/DAPI/Texas Red Triple Filter	1

* Filter cubes are available upon request, please specify the name of the microscope manufacturer and model name/number.

Index by Chromosome

Chromosome Region	Probe Name	Control Region	Cat. No.	Page No.
1-22 X, Y	Painting Probes - Aquarius®	–	LPP xxR/G	151
1-22 X, Y	Painting Probes - Chromoprobe Multiprobe® OctoChrome™	–	PMP 80x	152
1-22, X, Y	Satellite Enumeration Probes - Aquarius®	–	LPE xxxR/G	155
1-22, X, Y	Subtelomere Specific Probes - Aquarius®	–	LPT xxxP/Q, R/G	159
1-22 X, Y	Subtelomere Specific Probes - Chromoprobe Multiprobe®-T System	–	PMP 00x	162
1-22 X,Y	Aquarius TeloMark Kit	–	LPT MRK/LPT MRKxx	161
1p36.33	Monosomy 1p36	1qter	LPU 020	136
1p36.31	SRD (CHD5) Deletion	ZNF672	LPS 010	116
1p36.13	PAX7 Breakapart	–	LPS 013	113
1p36.32	1p36/1q25 and 19q13/19p13 Deletion Probe Kit	1q25.2	LPS 047	100
1p32.3/1q21.3	CKS1B/CDKN2C (P18) Amplification/Deletion	–	LPH 039	25
1q21.3/1p32.3	CKS1B/CDKN2C (P18) Amplification/Deletion	–	LPH 039	25
1q23.3/19p13.3	E2A (TCF3)/PBX1 Translocation, Dual Fusion	–	LPH 079	37
1q23.3/17q22/19p13.3	E2A (TCF3)/PBX1/HLF Translocation, Dual Fusion	–	LPH 080	38
1q25.2	1p36/1q25 and 19q13/19p13 Deletion Probe Kit	1q25.2	LPS 047	100
2p24.3/2q11.2	N-MYC (MYCN) Amplification AFF3	(2q11.2)	LPS 009	112
2p23.2-p23.1	ALK Breakapart	–	LPS 019	101
2p21	EML4 Breakapart	–	LPS 020	105
2p11.2	IGK Breakapart	–	LPH 034	51
2p11.2	IGK Breakapart (Haematopathology)	–	LPS 038	91
2q36.1	PAX3 Breakapart	–	LPS 012	113
3q26.2	EVI1 (MECOM) Breakapart	–	LPH 036	39
3q27.3	BCL6 Breakapart	–	LPH 035	21
3q27.3-q28	BCL6 Breakapart (Haematopathology)	–	LPS 029	84
4p16.3	Wolf-Hirschhorn	4qter	LPU 009	146
4p16.3/14q32.33	IGH/FGFR3 *Plus* Translocation, Dual Fusion	–	LPH 074	47
4q12	FIP1L1/CHIC2/PDGFRA Deletion/Fusion	–	LPH 032	40
4q21.3-q22.1/11q23.3	MLL (KMT2A)/AFF1 Translocation, Dual Fusion	–	LPH 081	53
5p15.31/5q31.2	Del(5q) Deletion	5p15.31	LPH 024	33
5p15.31/5p15.2/5q35	Cri-du-chat & Sotos Probe Combination	–	LPU 013	130
5p15.2/5p15.31/5q35	Cri-du-chat & Sotos Probe Combination	–	LPU 013	130
5q31.2/5p15.31	Del(5q) Deletion	5p15.31	LPH 024	33
5q32	PDGFRB Breakapart	–	LPH 031	60
5q35/5p15.31/5p15.2	Cri-du-chat & Sotos Probe Combination	–	LPU 013	130
5q35.1	TLX3 Breakapart	–	LPH 050	69
6p21/14q32.33	IGH/CCND3 *Plus* Translocation, Dual Fusion	–	LPH 075	45
6q22.1	ROS1 Breakapart	–	LPS 022	115
6q23.3	MYB Deletion	D6Z1	LPH 016	56
6q27/11q23.3	MLL/MLLT4 Translocation, Dual Fusion	–	RU-LPH 084	54
7p21.1/7q11.23	Saethre-Chotzen/Williams-Beuren Combination	–	LPU 024	140
7p11.2	EGFR Amplification	D7Z1	LPS 003	104
7q11.23	Williams-Beuren	D7Z1	LPU 011	145
7q11.23/7p21.1	Saethre-Chotzen/Williams-Beuren Combination	–	LPU 024	140
7q22.1-q22.2/7q31.2	Del(7q) Deletion	–	LPH 025	34
7q31.2/7q22.1-q22.2	Del(7q) Deletion	–	LPH 025	34
7q31.2	C-MET (MET) Amplification	D7Z1	LPS 004	103
7q34	TCRB (TRB) Breakapart	–	LPH 048	66
8p11.23-p11.22	FGFR1 Breakapart/Amplification	D8Z2	LPS 018	109
8q12.1-q12.2	CHARGE	D8Z2	LPU 021	129
8q21.3/21q22.12	AML1/ETO (RUNX1/RUNX1T1) Translocation, Dual Fusion	–	LPH 026	19
8q23.3/8q24.11	Langer-Giedion	D8Z2	LPU 022	135
8q24.11/8q23.3	Langer-Giedion	D8Z2	LPU 022	135
8q24.21	cMYC (MYC) Breakapart	–	LPH 010	28
8q24.21	MYC Breakapart (Haematopathology)	–	LPS 027	93
8q24.21/14q32.33	IGH/cMYC(MYC) Plus Translocation, Dual Fusion	–	LPH 076	46
8q24.21/14q32.33	IGH/MYC Translocation, Dual Fusion (Haematopathology)	–	LPS 035	90
9p21.3/11q23.3	MLL/MLLT3 Translocation, Dual Fusion	–	RU-LPH 083	54

Cytocell
an OGT company

Chromosome Region	Probe Name	Control Region	Cat. No.	Page No.
9p21.3	P16 (CDKN2A) Deletion	D9Z3	LPH 009	57
9p21.3	P16 (CDKN2A) Deletion (Haematopathology)	D9Z3	LPS 036	94
9q34.11-q34.12/22q11.22-q11.23	BCR/ABL (ABL1) Translocation, Dual Fusion	–	LPH 007	22
9q34.11-q34.12/22q11.22-q11.23	BCR/ABL (ABL1) *Plus* Translocation, Dual Fusion	–	LPH 038	23
10p14	DiGeorge II (10p14)	D10Z1	LPU 015	131
10q24.31	TLX1 Breakapart	–	LPH 049	68
11q13.3	CCND1 Breakapart (Haematopathology)	–	LPS 030	85
11q13.3/14q32.33	IGH/CCND1 *Plus* Translocation, Dual Fusion	–	LPH 072	44
11q13.3/14q32.33	IGH/CCND1 Translocation, Dual Fusion (Haematopathology)	–	LPS 031	88
11q13.3/14q32.33	IGH/MYEOV *Plus* Translocation, Dual Fusion	–	LPH 078	50
11q22.3	ATM Deletion	D11Z1	LPH 011	20
11q22.3/17p13.1	P53 (TP53)/ATM Probe Combination	–	LPH 052	59
11q23.3	MLL (KMT2A) Breakapart	–	LPH 013	52
11q23.3/4q21.3-q22.1	MLL (KMT2A)/AFF1 Translocation, Dual Fusion	–	LPH 081	53
11q23.3/6q27	MLL/MLLT4 Translocation, Dual Fusion	–	RU-LPH 084	54
11q23.3/9p21.3	MLL/MLLT3 Translocation, Dual Fusion	–	RU-LPH 083	54
11q23.3/19p13.3	MLL/MLLT1 Translocation, Dual Fusion	–	RU-LPH 082	54
11q24.3/22q12.1-q12.2	FLI1/EWSR1 Translocation, Dual Fusion	–	LPS 007	108
12p13.2/21q22.12	TEL/AML1 (ETV6/RUNX1) Translocation, Dual Fusion	–	LPH 012	67
12p11.1-q11.1	Alpha Satellite 12 *Plus* for CLL	–	LPH 069	27
12q13.3	CHOP (DDIT3) Breakapart	–	LPS 015	102
12q15	MDM2 Amplification	D12Z1	LPS 016	111
13q14.2-q14.3	13q14.3 Deletion	D13S1825	LPH 006	30
13q14.2-14.3	D13S319 *Plus* Deletion	LAMP1	LPH 068	30
13q14.2-14.3/12cen	D13S319/13qter/12cen Deletion/Enumeration	LAMP1	LPH 066	32
13q14.2	RB1 Deletion	LAMP1	LPS 011	96
13q14.3	D13S25 Deletion	D13S1825	LPH 043	30
14q11.2	TCRAD Breakapart	–	LPH 047	65
14q32.13-q32.2	TCL1 Breakapart	–	LPH 046	64
14q32.33	IGH Breakapart	–	LPH 014	41
14q32.33	IGH *Plus* Breakapart	–	LPH 070	42
14q32.33	IGH Breakapart (Haematopathology)	–	LPS 032	86
14q32.33/11q13.3	IGH/CCND1 *Plus* Translocation, Dual Fusion	–	LPH 072	44
14q32.33/11q13.3	IGH/CCND1 Translocation, Dual Fusion (Haematopathology)	–	LPS 031	88
14q32.33/11q13.3	IGH/MYEOV *Plus* Translocation, Dual Fusion	–	LPH 078	50
14q32.33/16q23.1-q23.2	IGH/MAF *Plus* Translocation, Dual Fusion	–	LPH 073	48
14q32.33/18q21.31-q21.32	IGH/MALT1 Translocation, Dual Fusion (Haematopathology)	–	LPS 034	89
14q32.33/18q21.33	IGH/BCL2 *Plus* Translocation, Dual Fusion	–	LPH 071	43
14q32.33/18q21.33-q22.1	IGH/BCL2 Translocation, Dual Fusion (Haematopathology)	–	LPS 033	87
14q32.33/20q12	IGH/MAFB *Plus* Translocation, Dual Fusion	–	LPH 077	49
14q32.33/4p16.3	IGH/FGFR3 *Plus* Translocation, Dual Fusion	–	LPH 074	47
14q32.33/6p21	IGH/CCND3 *Plus* Translocation, Dual Fusion	–	LPH 075	45
14q32.33/8q24.21	IGH/cMYC (MYC) *Plus* Translocation, Dual Fusion	–	LPH 076	46
14q32.33/8q24.21	IGH/MYC Translocation, Dual Fusion (Haematopathology)	–	LPS 035	90
15q11.2	Prader-Willi/Angelman (SNRPN)	15qter	LPU 005	138
15q11.2-q12	Angelman (UBE3A/D15S10)	15qter	LPU 006	128
15q24.1/17q21.1-q21.2	*FAST* PML/RARα (RARA) Translocation, Dual Fusion	–	LPH 064	61
15q24.1/17q21.1-q21.2	PML/RARα (RARA) Translocation, Dual Fusion	–	LPH 023	62
16p13.3	Rubinstein-Taybi	D16Z2	LPU 023	139
16p13.11/16q22.1	CBFβ/MYH11 Translocation, Dual Fusion	–	LPH 022	24
16q22.1/16p13.11	CBFβ/MYH11 Translocation, Dual Fusion	–	LPH 022	24
16q23.1-q23.2/14q32.33	IGH/MAF *Plus* Translocation, Dual Fusion	–	LPH 073	48
17p13.3/17p11.2	Smith-Magenis(FLII)/Miller-Dieker Probe Combination	–	LPU 007	142
17p13.3/17p11.2	Smith-Magenis(RAI1)/Miller-Dieker Probe Combination	–	LPU 019	142
17p13.1	P53 (TP53) Deletion	D17Z1	LPH 017	58
17p13.1	P53 (TP53) Deletion (Haematopathology)	D17Z1	LPS 037	95
17p13.1/11q22.3	P53 (TP53)/ATM Probe Combination	–	LPH 052	59

Chromosome Region	Probe Name	Control Region	Cat. No.	Page No.
17p11.2/17p13.3	Smith-Magenis (FLII)/Miller-Dieker Probe Combination	–	LPU 007	142
17p11.2/17p13.3	Smith-Magenis (RAI1)/Miller-Dieker Probe Combination	–	LPU 019	142
17q11.2	Neurofibromatosis Type 1	17pter	LPU 017	137
17q12	HER2 (ERBB2) Amplification	D17Z1	LPS 001	110
17q21.1-q21.2	RARα (RARA) Breakapart	–	LPH 065	63
17q21.1-q21.2/15q24.1	*FAST* PML/RARα (RARA) Translocation, Dual Fusion	–	LPH 064	61
17q21.1-q21.2/15q24.1	PML/RARα (RARA) Translocation, Dual Fusion	–	LPH 023	62
17q21.2	TOP2A Amplification/Deletion	D17Z1	LPS 002	119
17q22/1q23.3/19p13.3	E2A (TCF3)/PBX1/HLF Translocation, Dual Fusion	–	LPH 080	38
18q11.2	SYT (SS18) Breakapart	–	LPS 014	117
18q21.31-q21.32	MALT1 Breakapart	–	LPS 017	92
18q21.31-q21.32/14q32.33	IGH/MALT1 Translocation, Dual Fusion (Haematopathology)	–	LPS 034	89
18q21.33-q22.1	BCL2 Breakapart (Haematopathology)	–	LPS 028	83
18q21.33/14q32.33	IGH/BCL2 *Plus* Translocation, Dual Fusion	–	LPH 071	43
18q21.33-q22.1/14q32.33	IGH/BCL2 Translocation, Dual Fusion (Haematopathology)	–	LPS 033	87
19p13.3/11q23.3	MLL/MLLT1 Translocation, Dual Fusion	–	RU-LPH 082	54
19p13.2	1p36/1q25 and 19q13/19p13 Deletion Probe Kit	19p13.2	LPS 047	100
19p13.3	E2A (TCF3) Breakapart	–	LPH 019	36
19p13.3/1q23.3	E2A (TCF3)/PBX1 Translocation, Dual Fusion	–	LPH 079	37
19p13.3/1q23.3/17q22	E2A/PBX1/HLF Translocation, Dual Fusion	–	LPH 080	38
19q13.33	1p36/1q25 and 19q13/19p13 Deletion Probe Kit 1	9p13.2	LPS 047	100
20p12.2	Alagille (JAG1)	20qter	LPH 012	127
20q12.2/14q32.33	IGH/MAFB *Plus* Translocation, Dual Fusion	–	LPH 077	49
20q12/20q13.12	Del(20q) Deletion	–	LPH 020	35
20q13.12/20q12	Del(20q) Deletion	–	LPH 020	35
20q13.2	ZNF217 Amplification	DEFB128	LPS 005	120
21q22.12	AML1 (RUNX1) Breakapart	–	LPH 027	18
21q22.12/12p13.2	TEL/AML1 (ETV6/RUNX1) Translocation, Dual Fusion	–	LPH 012	67
21q22.12/8q21.3	AML1/ETO (RUNX1/RUNX1T1) Translocation, Dual Fusion	–	LPH 026	19
21q22.13-q22.2/21q22.2-q22.3	TMPRSS2/ERG Deletion/Breakapart	ERG (21q22.2)	LPS 021	118
21q22.13-q22.2/22q12.1-q12.2	EWSR1/ERG Translocation, Dual Fusion	–	LPS 008	107
21q22.2-q22.3/21q22.13-q22.2	TMPRSS2/ERG Deletion/Breakapart	ERG (21q22.2)	LPS 021	118
22q11.21-q11.23	IGL Breakapart	–	LPH 033	51
22q11.21-q11.23	IGL Breakapart (Haematopathology)	–	LPS 039	91
22q11.21/22q13.33	DiGeorge TBX1 & 22q13.3 Deletion Syndrome Probe Combination	–	LPU 014	132
22q11.21/22q13.33	DiGeorge/VCFS N25 & 22q13.3 Deletion Syndrome Probe Combination	–	LPU 010	132
22q11.21/22q13.33	DiGeorge/VCFS TUPLE1 & 22q13.3 Deletion Syndrome Probe Combination	–	LPU 004	132
22q11.22-q11.23/9q34.11-q34.12	BCR/ABL (ABL1) Translocation, Dual Fusion	–	LPH 007	22
22q11.22-q11.23/9q34.11-q34.12	BCR/ABL (ABL1) *Plus* Translocation, Dual Fusion	–	LPH 038	23
22q12.1-q12.2	EWSR1 Breakapart	–	LPS 006	106
22q12.1-q12.2/11q24.3	FLI1/EWSR1 Translocation, Dual Fusion	–	LPS 007	108
22q12.1-q12.2/21q22.13-q22.2	EWSR1/ERG Translocation, Dual Fusion	–	LPS 008	107
22q13.33/22q11.21	DiGeorge TBX1 & 22q13.3 Deletion Syndrome Probe Combination	–	LPU 014	132
22q13.33/22q11.21	DiGeorge/VCFS N25 & 22q13.3 Deletion Syndrome Probe Combination	–	LPU 010	132
22q13.33/22q11.21	DiGeorge/VCFS TUPLE1 & 22q13.3 Deletion Syndrome Probe Combination	–	LPU 004	132
Xp22.33/Yp11.32	CRLF2 Breakapart	–	RU-LPH 085	29
Xp22.33/Yp11.32	SHOX	DXZ1, DYZ1	LPU 025	141
Xp22.33/Yp11.32	P2RY8 Deletion	–	RU-LPH 086	29
Xp22.31	Kallmann (KAL1) & Steroid Sulphatase Deficiency (STS) Probe Combination	DXZ1	LPU 016	134
Xp11.1-q11.1/Yp11.1-q11.1	Dual labelled Satellite Probe Set XYc	–	LPE 0XYc	156
Xp11.1-q11.1/Yq12	Dual labelled Satellite Probe Set XYq	–	LPE 0XYq	156
Xq13.2	XIST	DXZ1	LPU 018	147
Yp11.32/Xp22.33	CRLF2 Breakapart	–	RU-LPH 085	29

Cytocell
an OGT company

Index by Gene Name

HGNC Gene Name	Chromosome Region	Product Name	Cat. No.	Page No.
ABL1	9q34.12	BCR/ABL (ABL1) Translocation Dual Fusion	LPH 007	22
		BCR/ABL (ABL1) *Plus* Translocation Dual Fusion	LPH 038	23
		Chromoprobe Multiprobe® ALL v2	PMP 03x	74
AFF1	4q21.3-q22.1	MLL (KMT2A)/AFF1 Translocation, Dual Fusion	LPH 081	53
ALK	2p23.2-p23.1	ALK Breakapart	LPS 019	101
ANGPTL1	1q25.2	1p36/1q25 and 19q13/19p13 Deletion Probe Kit	LPS 047	100
ANOS1	Xp22.31	Kallmann (KAL1) Region/STS Region	LPU 016	134
ASS1	9q34.12	BCR/ABL (ABL1) Translocation, Dual Fusion	LPH 007	22
ATM	11q22.3	ATM Deletion	LPH 011	20
		P53 (TP53)/ATM Probe Combination	LPH 052	59
		CLL PROFILER Kit	LPH 067	26
		CLL *Plus* Screening Panel	LPH 087	27
		Chromoprobe Multiprobe® CLL	PMP 01x	76
BCL2	18q21.33	BCL2 Breakapart (Haematopathology)	LPS 028	83
		IGH/BCL2 *Plus* Translocation, Dual Fusion	LPH 071	43
		IGH/BCL2 Translocation, Dual Fusion (Haematopathology)	LPS 033	87
		Chromoprobe Multiprobe® CLL	PMP 01x	76
BCL6	3q27.3	BCL6 Breakapart	LPH 035	21
		BCL6 Breakapart (Haematopathology)	LPS 029	84
BCR	22q11.23	BCR/ABL (ABL1) Translocation Dual Fusion	LPH 007	22
		BCR/ABL (ABL1) *Plus* Translocation Dual Fusion	LPH 038	23
		Chromoprobe Multiprobe® ALL v2	PMP 03x	74
CBFB	16q22.1	CBFβ/MYH11 Translocation, Dual Fusion	LPH 022	24
		Chromoprobe Multiprobe® AML/MDS	PMP 02x	78
CCND1	11q13.3	CCND1 Breakapart (Haematopathology)	LPS 030	85
		IGH/CCND1 *Plus* Translocation, Dual Fusion	LPH 072	44
		IGH/CCND1 Translocation, Dual Fusion (Haematopathology)	LPS 031	88
		Chromoprobe Multiprobe® CLL	PMP 01x	76
CCND3	6p21.1	IGH/CCND3 *Plus* Translocation, Dual Fusion	LPH 075	45
CDKN2A	9p21.3	P16 (CDKN2A) Deletion	LPH 009	57
		P16 (CDKN2A) Deletion (Haematopathology)	LPS 036	94
		Chromoprobe Multiprobe® ALL v2	PMP 03x	74
CDKN2C	1p32.3	CKS1B/CDKN2C (P18) Amplification/Deletion	LPH 039	25
CELF2	10p14	DiGeorge II (10p14)	LPU 015	131
CHD5	1p36.31	SRD (CHD5) Deletion	LPS 010	116
CHD7	8q12.1-q12.2	CHARGE	LPU 021	129
CHIC2	4q12	FIP1L1/CHIC2/PDGFRA Deletion/Fusion	LPH 032	40
CKS1B	1q21.3	CKS1B/CDKN2C(P18) Amplification/Deletion	LPH 039	25
CREBBP	16p13.3	Rubinstein-Taybi	LPU 023	139
CRLF2	Yp11.32/Xp22.33	CRLF2 Breakapart	RU-LPH 085	29
DLEU1	13q14.2-14.3	D13S319 *Plus* Deletion	LPH 068	30
		D13S319/13qter/12cen Deletion/Enumeration	LPH 066	32
		13q14.3	LPH 006	30
		CLL PROFILER Kit	LPH 067	26
		CLL *Plus* Screening Panel	LPH 087	27
		Chromoprobe Multiprobe® CLL	PMP 01x	76
DLEU2	13q14.2-14.3	D13S319 *Plus* Deletion	LPH 068	30
		D13S319/13qter/12cen Deletion/Enumeration	LPH 066	32
		13q14.2	LPH 006	30
		CLL PROFILER Kit	LPH 067	26
		CLL *Plus* Screening Panel	LPH 087	27
		Chromoprobe Multiprobe® CLL	PMP 01x	76
DLEU7	13q14.3	D13S25 Deletion	LPH 043	30
DDIT3	12q13.3	CHOP (DDIT3) Breakapart	LPS 015	102
EGFR	7p11.2	EGFR Amplification	LPS 003	104
EGR1	5q31.2	Del(5q) Deletion	LPH 024	33

HGNC Gene Name	Chromosome Region	Product Name	Cat. No.	Page No.
ELN	7q11.23	Williams-Beuren	LPU 011	145
	7q11.23	Saethre-Chotzen/Williams-Beuren Combination	LPU 024	140
EML4	2p21	EML4 Breakapart	LPS 020	105
ERBB2	17q12	HER2 (ERBB2) Amplification	LPS 001	110
ERG	21q22.13-q22.2	TMPRSS2/ERG Deletion/Breakapart	LPS 021	118
ETV6	12p13.2	TEL/AML1 (EVT6/RUNX1) Translocation, Dual Fusion	LPH 012	67
		Chromoprobe Multiprobe® ALL v2	PMP 03x	74
EWSR1	22q12.2	EWSR1 Breakapart	LPS 006	106
		FLI1/EWSR1 Translocation, Dual Fusion	LPS 007	108
		EWSR1/ERG Translocation, Dual Fusion	LPS 008	107
EXT1	8q24.11	Langer-Giedion	LPU 022	135
FGFR1	8p11.23-p11.22	FGFR1 Breakapart/Amplification	LPS018	108
FGFR3	4p16.3	IGH/FGFR3 *Plus* Translocation, Dual Fusion	LPH 074	46
FIP1L1	4q12	FIP1L1/CHIC2/PDGFRA Deletion/Fusion	LPH 032	40
FLI1	11q24.3	FLI1/EWSR1 Translocation, Dual Fusion	LPS 007	108
FLII	17p11.2	Smith-Magenis (FLII)/Miller-Dieker Probe Combination	LPU 007	142
GLTSCR1/GLTSCR2	19q13.33	1p36/1q25 and 19q13/19p13 Deletion Probe Kit	LPS 047	100
HIRA	22q11.21	DiGeorge/VCFS TUPLE1 & 22q13.3 Deletion Syndrome Probe Combinations	LPU004	132
HLF	17q22	E2A (TCF3)/PBX1/HLF Translocation, Dual Fusion	LPH 080	38
IGH	14q32.33	IGH Breakapart	LPH 014	41
		IGH *Plus* Breakapart	LPH 070	42
		IGH Breakapart (Haematopathology)	LPS 032	86
		IGH/BCL2 *Plus* Translocation, Dual Fusion	LPH 071	43
		IGH/BCL2 Translocation, Dual Fusion (Haematopathology)	LPS 033	87
		IGH/CCND1 *Plus* Translocation, Dual Fusion	LPH 072	44
		IGH/CCND1 Translocation, Dual Fusion (Haematopathology)	LPS 031	88
		IGH/CCND3 *Plus* Translocation, Dual Fusion	LPH 075	45
		IGH/cMYC (MYC) *Plus* Translocation, Dual Fusion	LPH 076	46
		IGH/FGFR3 *Plus* Translocation, Dual Fusion	LPH 074	47
		IGH/MAF *Plus* Translocation, Dual Fusion	LPH 073	48
		IGH/MAFB *Plus* Translocation, Dual Fusion	LPH 077	49
		IGH/MALT1 Translocation, Dual Fusion (Haematopathology)	LPS 034	89
		IGH/MYC Translocation, Dual Fusion (Haematopathology)	LPS 035	90
		IGH/MYEOV *Plus* Translocation, Dual Fusion	LPH 078	50
		Chromoprobe Multiprobe® ALL v2	PMP 03x	74
		Chromoprobe Multiprobe® CLL	PMP 01x	76
IGK	2p11.2	IGK Breakapart	LPH 034	51
		IGK Breakapart (Haematopathology)	LPS 038	91
IGL	22q11.21-q11.23	IGL Breakapart	LPH 033	51
		IGL Breakapart (Haematopathology)	LPS 039	91
JAG1	20p12.2	Alagille (JAG1)	LPU 012	127
KMT2A	11q23.3	MLL (KMT2A) Breakapart	LPH 013	52
		MLL (KMT2A)/AFF1 Translocation, Dual Fusion	LPH 081	53
		MLL/MLLT1 Translocation, Dual Fusion	RU-LPH 082	54
		MLL/MLLT3 Translocation, Dual Fusion	RU-LPH 083	54
		MLL/MLLT4 Translocation, Dual Fusion	RU-LPH 084	54
		Chromoprobe Multiprobe® ALL v2	PMP 03x	74
		Chromoprobe Multiprobe® AML/MDS	PMP 02x	78
MAF	16q23.2	IGH/MAF *Plus* Translocation, Dual Fusion	LPH 073	48
MAFB	20q12	IGH/MAFB *Plus* Translocation, Dual Fusion	LPH 077	49
MALT1	18q21.32	MALT1 Breakapart	LPS 017	92
		IGH/MALT1 Translocation, Dual Fusion (Haematopathology)	LPS 034	89
MDM2	12q15	MDM2 Amplification	LPS 016	111
MECOM	3q26.2	EVI1 (MECOM) Breakapart	LPH 036	39
MET	7q31.2	C-MET (MET) Amplification	LPS 004	103
MLLT1	19p13.3	MLL/MLLT1 Translocation, Dual Fusion	RU-LPH 082	54

HGNC Gene Name	Chromosome Region	Product Name	Cat. No.	Page No.
MLLT3	9p21.3	MLL/MLLT3 Translocation, Dual Fusion	RU-LPH 083	54
MLLT4	6q27	MLL/MLLT4 Translocation, Dual Fusion	RU-LPH 084	54
MYB	6q23.3	MYB Deletion	LPH 016	56
		CLL *Plus* Screening Panel	LPH 087	27
		Chromoprobe Multiprobe® CLL	PMP 01x	76
MYBL2	20q13.12	Del(20q) Deletion	LPH 020	35
MYC	8q24.21	cMYC (MYC) Breakapart	LPH 010	28
		MYC Breakapart (Haematopathology)	LPS 027	93
		IGH/cMYC (MYC) *Plus* Translocation, Dual Fusion	LPH 076	46
		IGH/MYC Translocation, Dual Fusion (Haematopathology)	LPS 035	90
		ALL-Chromoprobe Multiprobe®	PMP 03x	74
MYCN	2p24.3	N-MYC (MYCN) Amplification	LPS 009	112
MYEOV	11q13.3	IGH/MYEOV *Plus* Translocation, Dual Fusion	LPH 078	49
MYH11	16p13.11	CBFβ/MYH11 Translocation, Dual Fusion	LPH 022	24
		Chromoprobe Multiprobe® AML/MDS	PMP 02x	78
NF1	17q11.2	Neurofibromatosis Type 1	LPU 017	137
NSD1	5q35.2-q35.3	Cri-du-chat & Sotos Probe Combination	LPU 013	130
P2RY8	Yp11.32/Xp22.33	P2RY8 Deletion	RU-LPH 060	29
PAX3	2q36.1	PAX3 Breakapart	LPS 012	113
PAX7	1p36.13	PAX7 Breakapart	LPS 013	113
PBX1	1q23.3	E2A/PBX1 Translocation, Dual Fusion	LPH 079	37
		E2A/PBX1/HLF Translocation, Dual Fusion	LPH 080	38
PDGFRA	4q12	FIP1L1/CHIC2/PDGFRA Deletion/Fusion	LPH 032	40
PDGFRB	5q32	PDGFRB Breakapart	LPH 031	60
PML	15q24.1	*FAST* PML/RARα (RARA) Translocation, Dual Fusion	LPH 064	61
		PML/RARα (RARA) Translocation, Dual Fusion	LPH 023	62
		Chromoprobe Multiprobe® AML/MDS	PMP 02x	78
RAI1	17p11.2	Smith-Magenis (RAI1)/Miller-Dieker Probe Combination	LPU 019	142
RARA	17q21.1-q21.2	*FAST* PML/RARα (RARA) Translocation, Dual Fusion	LPH 064	61
		PML/RARα (RARA) Translocation, Dual Fusion	LPH 023	62
		RARα (RARA) Breakapart	LPH 065	63
		Chromoprobe Multiprobe® AML/MDS	PMP 02x	78
RELN	7q22.2	Del(7q) Deletion	LPH 025	34
RB1	13q14.2	RB1 Deletion	LPS 011	96
ROS1	6q22.1	ROS1 Breakapart	LPS 022	115
RUNX1	21q22.12	AML1 (RUNX1) Breakapart	LPH 027	18
		AML1/ETO (RUNX1/RUNX1T1) Translocation, Dual Fusion	LPH 026	19
		TEL/AML1 (ETV6/RUNX1) Translocation, Dual Fusion	LPH 012	67
		Chromoprobe Multiprobe® ALL v2	PMP 03x	74
		Chromoprobe Multiprobe® AML/MDS	PMP 02x	78
RUNX1T1	8q21.3	AML1/ETO (RUNX1/RUNX1T1) Translocation, Dual Fusion	LPH 026	19
		Chromoprobe Multiprobe® AML/MDS	PMP 02x	78
SHOX	Xp22.33/Yp11.32	SHOX	LPU 025	141
SNRPN	15q11.2	Prader-Willi/Angelman (SNRPN)	LPU 005	138
SRY	Yp11.31	SRY	LPU 026	144
SS18	18q11.2	SYT (SS18) Breakapart	LPS 014	117
STS	Xp22.31	Kallmann (KAL1) & Steroid Sulphatase Deficiency (STS) Probe Combination	LPU016	134
TBX1	22q11.21	DiGeorge TBX1 & 22q13.3 Deletion Syndrome Probe Combination	LPU 014	132
TCF3	19p13.3	E2A (TCF3) Breakapart	LPH 019	36
		E2A/PBX1 Translocation, Dual Fusion	LPH 079	37
		E2A/PBX1/HLF Translocation, Dual Fusion	LPH 080	38
		Chromoprobe Multiprobe® ALL v2	PMP 03x	74
TCL1 A/B	14q32.13-q32.2	TCL1 Breakapart	LPH 046	64
TLX1	10q24.31	TLX1 Breakapart	LPH 049	68
TLX3	5q35.1	TLX3 Breakapart	LPH 050	69

HGNC Gene Name	Chromosome Region	Product Name	Cat. No.	Page No.
TMPRSS2	21q22.2-q22.3	TMPRSS2/ERG Deletion/Breakapart	LPS 021	118
TOP2A	17q21.2	TOP2A Amplification/Deletion	LPS 002	119
TP53	17p13.1	P53 (TP53) Deletion	LPH 017	58
		P53 (TP53) Deletion (Haematopathology)	LPS 037	95
		P53 (TP53)/ATM Probe Combination	LPH 052	59
		CLL PROFILER Kit	LPH 067	26
		CLL *Plus* Screening Panel	LPH 087	27
		Chromoprobe Multiprobe® AML/MDS	PMP 02x	78
		Chromoprobe Multiprobe® CLL	PMP 01x	76
TP73	1p36.32	1p36/1q25 and 19q13/19p13 Deletion Probe Kit	LPS 047	100
TRA	14q11.2	TCRAD Breakapart	LPH 047	65
TRB	7q34	TCRB (TRB) Breakapart	LPH 048	66
TRD	14q11.2	TCRAD Breakapart	LPH 047	65
TRPS1	8q23.3	Langer-Giedion	LPU 022	135
TWIST1	7p21.1	Saethre-Chotzen/Williams-Beuren Combination	LPU 024	140
UBE2QL1	5p15.31	Cri-du-chat & Sotos Probe Combination	LPU 013	130
UBE3A	15q11.2	Angelman (UBE3A/D15S10)	LPU 006	128
XIST	Xq13.2	XIST	LPU 018	147
ZNF217	20q13.2	ZNF217 Amplification	LPS 005	120
ZNF443	19p13.2	1p36/1q25 and 19q13/19p13 Deletion Probe Kit	LPS 047	100

Cytocell
an OGT company

Pathology Products by Disease State*

Malignancy	Chromosome Region	Cytocell Products	Cat. No.	Page No.
Brain Tumor	9p21.3	P16 (CDKN2A) Deletion	LPS 036	94
Breast Cancer	7q31.2	C-MET (MET) Amplification	LPS 004	103
	11q13.3	CCND1 Breakapart	LPS 030	85
	7p11.2	EGFR Amplification	LPS 003	104
	8p11.23-p11.22	FGFR1 Breakapart/Amplification	LPS 018	109
	17q12	HER2 (ERBB2) Amplification	LPS 001	110
	17p13.1	P53 (TP53) Deletion	LPS 037	95
	13q14.2	RB1 Deletion	LPS 011	96
	1p36.31	SRD (CHD5) Deletion	LPS 010	116
	17q21.2	TOP2A Amplification/Deletion	LPS 002	119
	20q13.2	ZNF217 Amplification	LPS 005	120
Cholangiocarcinoma (Bile duct)	6q22.1	ROS1 Breakapart	LPS 022	115
Colorectal Cancer	7q31.2	C-MET (MET) Amplification	LPS 004	103
	7p11.2	EGFR Amplification	LPS 003	104
	12q15	MDM2 Amplification	LPS 016	111
	1p36.31	SRD (CHD5) Deletion	LPS 010	116
Gallbladder Cancer	1p36.31	SRD (CHD5) Deletion	LPS 010	116
Gastric Cancer	11q13.3	CCND1 Breakapart	LPS 030	85
	17p13.1	P53 (TP53) Deletion	LPS 037	95
	1p36.31	SRD (CHD5) Deletion	LPS 010	116
Glioma	1p36.32/19q13.33	1p36/1q25 and 19q13/19p13 Deletion	LPS 047	100
	12q15	MDM2 Amplification	LPS 016	111
	6q22.1	ROS1 Breakapart	LPS 022	115
	1p36.31	SRD (CHD5) Deletion	LPS 010	116
Inflammatory Myofibroblastic Tumours	2p23.2-p23.1	ALK Breakapart	LPS 019	101
Laryngeal	1p36.31	SRD (CHD5) Deletion	LPS 010	116
Lung Cancer	7q31.2	C-MET (MET) Amplification	LPS 004	103
	17q12	HER2 (ERBB2) Amplification	LPS 001	110
	2p23.2-p23.1	ALK Breakapart	LPS 019	101
	2p21	EML4 Breakapart	LPS 020	105
	6q22.1	ROS1 Breakapart	LPS 022	115
	7p11.2	EGFR Amplification	LPS 003	104
	9p21.3	P16 (CDKN2A) Deletion	LPS 036	94
	17p13.1	P53 (TP53) Deletion	LPS 037	95
	13q14.2	RB1 Deletion	LPS 011	96
	8p11.23-p11.22	FGFR1 Breakapart/Amplification	LPS 018	109
	12q15	MDM2 Amplification	LPS 016	111
	1p36.31	SRD (CHD5) Deletion	LPS 010	116
Lymphoma	2p23.2-p23.1	ALK Breakapart	LPS 019	101
	18q21.33-q22.1	BCL2 Breakapart	LPS 028	83
	3q27.3-q28	BCL6 Breakapart	LPS 029	84
	11q13.3	CCND1 Breakapart	LPS 030	85
	14q32.33	IGH Breakapart	LPS 032	86
	14q32.33/18q21.33	IGH/BCL2 Translocation	LPS 033	87
	14q32.33/11q13.3	IGH/CCND1 Translocation	LPS 031	88
	14q32.33/18q21.31-q21.32	IGH/MALT1 Translocation	LPS 034	89
	14q32.33/8q24.21	IGH/MYC Translocation	LPS 035	90
	2p11.2	IGK Breakapart	LPS 038	91
	22q11.21-q11.23	IGL Breakapart	LPS 039	91
	18q21.31-q21.32	MALT1 Breakapart	LPS 017	92
	8q24.21	MYC Breakapart	LPS 027	93
	9p21.3	P16 (CDKN2A) Deletion	LPS 036	94
	1p36.31	SRD (CHD5) Deletion	LPS 010	116
	17p13.1	P53 (TP53) Deletion	LPS 037	95
Medulloblastoma	2p24.3	N-MYC (MYCN) Amplification	LPS 009	112

Malignancy	Chromosome Region	Cytocell Products	Cat. No.	Page No.
Neuroblastoma	2p24.3	N-MYC (MYCN) Amplification	LPS 009	112
	1p36.31	SRD (CHD5) Deletion	LPS 010	116
Oesophageal Cancer	2p23.2-p23.1	ALK Breakapart	LPS 019	101
	12q15	MDM2 Amplification	LPS 016	111
	13q14.2	RB1 Deletion	LPS 011	96
Ovarian Cancer	7q31.2	C-MET (MET) Amplification	LPS 004	103
	17q12	HER2 (ERBB2) Amplification	LPS 001	110
	6q22.1	ROS1 Breakapart	LPS 022	115
	1p36.31	SRD (CHD5) Deletion	LPS 010	116
	17q21.2	TOP2A Amplification/Deletion	LPS 002	119
	20q13.2	ZNF217 Amplification	LPS 005	120
Pancreatic Cancer	7q31.2	C-MET (MET) Amplification	LPS 004	103
Prostate Cancer	1p36.31	SRD (CHD5) Deletion	LPS 010	116
	21q22.2-q22.3/21q22.13-q22.2	TMPRSS2/ERG Deletion/Breakapart	LPS 021	118
	20q13.2	ZNF217 Amplification	LPS 005	120
Retinoblastoma	2p24.3	N-MYC (MYCN) Amplification	LPS 009	112
	13q14.2	RB1 Deletion	LPS 011	96
Salivary Gland	17q12	HER2 (ERBB2) Amplification	LPS 001	110
Sarcoma	7q31.2	c-MET (MET) Amplification	LPS 004	103
	12q13.3	CHOP (DDIT3) Breakapart	LPS 015	102
	22q12.1-q12.2	EWSR1 Breakapart	LPS 006	106
	22q12.1-q12.2/21q22.13-q22.2	EWSR1/ERG Translocation	LPS 008	107
	11q24.3/22q12.1-q12.2	FLI1/EWSR1 Translocation	LPS 007	108
	17q12	HER2 (ERBB2) Amplification	LPS 001	110
	12q15	MDM2 Amplification	LPS 016	111
	2q36.1	PAX3 Breakapart	LPS 012	113
	1p36.13	PAX7 Breakapart	LPS 013	113
	18q11.2	SYT (SS18) Breakapart	LPS 014	117
	20q13.2	ZNF217 Amplification	LPS 005	120
Thyroid Cancer	7q31.2	C-MET (MET) Amplification	LPS 004	103

* As supported by literature

Cytocell
an OGT company

Haematology Products by Disease State*

Haematological Malignancy	Chromosome Region	Cytocell Products	Cat. No.	Page No.
ALL Acute Lymphoblastic Leukaemia (ALL)	21q22.12	AML1 (RUNX1) Breakapart	LPH 027	18
	22q11.22-q11.23/9q34.11-q34.12	BCR/ABL (ABL1) Translocation	LPH 007	22
	22q11.22-q11.23/9q34.11-q34.12	BCR/ABL (ABL1) *Plus* Translocation	LPH 038	23
	19p13.3	E2A (TCF3) Breakapart	LPH 019	36
	19p13.3/1q23.3	E2A (TCF3)/PBX1 Translocation	LPH 079	37
	19p13.3/1q23.3/17q22	E2A (TCF3)/PBX1/HLF Translocation	LPH 080	38
	14q32.33	IGH Breakapart	LPH 014	41
	14q32.33	IGH *Plus* Breakapart	LPH 070	42
	11q23.3	MLL (KMT2A) Breakapart	LPH 013	52
	11q23.3/4q21.3-q22.1	MLL (KMT2A)/AFF1 Translocation	LPH 081	53
	11q23.3/19p13.3	MLL/MLLT1 Translocation	RU-LPH 082	54
	11q23.3/9p21.3	MLL/MLLT3 Translocation	RU-LPH 083	54
	11q23.3/6q27	MLL/MLLT4 Translocation	RU-LPH 084	54
	6q23.3	MYB Deletion	LPH 016	56
	5q32	PDGFRB Breakapart	LPH 031	60
	9p21.3	P16 (CDKN2A) Deletion	LPH 009	57
	17p13.1	P53 (TP53) Deletion	LPH 017	59
	14q32.13-q32.2	TCL1 Breakapart	LPH 046	64
	14q11.2	TCRAD Breakapart	LPH 047	65
	7q34	TCRB (TRB) Breakapart	LPH 048	66
	12p13.2/21q22.12	TEL/AML1 (ETV6/RUNX1) Translocation	LPH 012	67
	10q24.31	TLX1 Breakapart	LPH 049	68
	5q35.1	TLX3 Breakapart	LPH 050	69
	Xp22.33/Yp11.32	CRLF2 Breakapart	RU-LPH 085	29
	Xp22.33/Yp11.32	P2RY8 Deletion	RU-LPH 086	29
AML Acute Myeloid Leukaemia (AML)	21q22.12	AML1 (RUNX1) Breakapart	LPH 027	18
	21q22.12/8q21.3	AML1/ETO (RUNX1/RUNX1T1) Translocation	LPH 026	19
	22q11.22-q11.23/9q34.11-q34.12	BCR/ABL (ABL1) Translocation	LPH 007	22
	22q11.22-q11.23/9q34.11-q34.12	BCR/ABL (ABL1) *Plus* Translocation	LPH 038	23
	16q22.1/16p13.11	CBFβ/MYH11 Translocation	LPH 022	24
	5p15.31/5q31.2	Del(5q) Deletion	LPH 024	33
	7q22.1-q22.2/7q31.2	Del(7q) Deletion	LPH 025	34
	20q12/20q13.12	Del(20q) Deletion	LPH 020	35
	3q26.2	EVI1 (MECOM) Breakapart	LPH 036	39
	11q23.3	MLL (KMT2A) Breakapart	LPH 013	52
	11q23.3/4q21.3-q22.1	MLL (KMT2A)/AFF1 Translocation	LPH 081	53
	11q23.3/19p13.3	MLL/MLLT1 Translocation	RU-LPH 082	54
	11q23.3/9p21.3	MLL/MLLT3 Translocation	RU-LPH 083	54
	11q23.3/6q27	MLL/MLLT4 Translocation	RU-LPH 084	54
	17p13.1	P53 (TP53) Deletion	LPH 017	58
	15q24.1/17q21.1-q21.2	*FAST* PML/RARα (RARA) Translocation	LPH 064	61
	15q24.1/17q21.1-q21.2	PML/RARα (RARA) Translocation	LPH 023	62
	17q21.1-q21.2	RARα (RARA) Breakapart	LPH 065	63
CLL Chronic Lymphocytic Leukaemia (CLL)	13q14.2-q14.3	13q14.3 Deletion	LPH 006	30
	12p11.1-q11.1	Alpha Satellite 12 *Plus* for CLL	LPH 069	27
	11q22.3	ATM Deletion	LPH 011	20
	13q14.3	D13S25 Deletion	LPH 043	30
	13q14.2	D13S319 *Plus* Deletion	LPH 068	30
	13q14.2/12cen	D13S319/13qter/12cen Deletion/Enumeration	LPH 066	32
	14q32.33	IGH Breakapart	LPH014	41
	14q32.33	IGH *Plus* Breakapart	LPH 070	42
	14q32.33/18q21.33	IGH/BCL2 *Plus* Translocation	LPH 071	43

Haematological Malignancy	Chromosome Region	Cytocell Products	Cat. No.	Page No.
	6q23.3	MYB Deletion	LPH 016	56
	17p13.1	P53 (TP53) Deletion	LPH 017	58
	17p13.1/11q22.3	P53 (TP53)/ATM Probe Combination	LPH 052	59
	Various	CLL PROFILER Kit	LPH 067	26
	Various	CLL *Plus* Screening Panel	LPH 087	27
CML **Chronic Myeloid Leukaemia (CML)**	22q11.22-q11.23/9q34.11-q34.12	BCR/ABL (ABL1) Translocation	LPH 007	22
	22q11.22-q11.23/9q34.11-q34.12	BCR/ABL (ABL1) *Plus* Translocation	LPH 038	23
MDS **Myelodysplastic Syndrome (MDS)**	5p15.31/5q31.2	Del(5q) Deletion	LPH 024	33
	7q22.1-q22.2/7q31.2	Del(7q) Deletion	LPH 025	34
	20q12/20q13.12	Del(20q) Deletion	LPH 020	35
	3q26.2	EVI1 (MECOM) Breakapart	LPH 036	39
MPN **Myeloproliferative Neoplasm (MPN)**	4q12	FIP1L1/CHIC2/PDGFRA Deletion/Fusion	LPH 032	40
	5p15.31/5q31.2	Del(5q) Deletion	LPH 024	33
	5q32	PDGFRB Breakapart	LPH 031	60
	7q22.1-q22.2/7q31.2	Del(7q) Deletion	LPH 025	34
	20q12/20q13.12	Del(20q) Deletion	LPH 020	35
L **Lymphoma (L)**	3q27.3	BCL6 Breakapart	LPH 035	21
	8q24.21	cMYC (MYC) Breakapart	LPH 010	28
	14q32.33	IGH Breakapart	LPH 014	41
	14q32.33	IGH *Plus* Breakapart	LPH 070	42
	14q32.33/18q21.33	IGH/BCL2 *Plus* Translocation	LPH 071	43
	14q32.33/11q13.3	IGH/CCND1 *Plus* Translocation	LPH 072	44
	14q32.33/6p21	IGH/CCND3 *Plus* Translocation	LPH 075	45
	14q32.33/8q24.21	IGH/cMYC (MYC) *Plus* Translocation	LPH 076	46
	2p11.2	IGK Breakapart	LPH 034	51
	22q11.21-q11.23	IGL Breakapart	LPH 033	51
	6q23.3	MYB Deletion	LPH 016	56
	9p21.3	P16 (CDKN2A)	LPH 009	57
	17p13.1	P53 (TP53) Deletion	LPH 017	58
MM **Multiple Myeloma (MM)**	13q14.2-q14.3 13q14.3	Deletion LPH 006 30		
	1q21.3/1p32.3	CKS1B/CDKN2C(P18) Amplification/Deletion	LPH 039	25
	13q14.3	D13S25 Deletion	LPH 043	30
	13q14.2	D13S319 *Plus* Deletion	LPH 068	30
	13q14.2/12cen	D13S319/13qter/12cen Deletion/Enumeration	LPH 066	32
	14q32.33	IGH Breakapart	LPH 014	41
	14q32.33	IGH *Plus* Breakapart	LPH 070	42
	14q32.33/11q13.3	IGH/CCND1 *Plus* Translocation	LPH 072	43
	14q32.33/6p21	IGH/CCND3 *Plus* Translocation	LPH 075	45
	14q32.33/4p16.3	IGH/FGFR3 *Plus* Translocation	LPH 074	47
	14q32.33/16q23.1-q23.2	IGH/MAF *Plus* Translocation	LPH 073	48
	14q32.33/20q12	IGH/MAFB *Plus* Translocation	LPH 077	49
	14q32.33/11q13.3	IGH/MYEOV *Plus* Translocation	LPH 078	50
	17p13.1	P53 (TP53) Deletion	LPH 017	59

* As supported by literature

Notes

Notes

Notes

Put our expertise to work for you

Custom solutions to advance your research

myProbes® FISH Probes – Our custom design and manufacture service provides unique FISH probes using the BAC-2-FISH™ process. This process utilises the proprietary Cytocell BAC clone collection containing >220,000 clones to produce fully quality-assured custom FISH probes for virtually any sequence in the entire human genome.

SureSeq myPanel™ NGS Custom Cancer Panels – Create a custom cancer panel from our regularly updated, expert-curated library of pre-optimised cancer panel content. Simply mix and match the gene, exonic or intronic content you need to create an NGS cancer panel that meets your exact requirements.

Custom CytoSure™ Arrays – Take advantage of our extensive array design experience and unique probe design pipeline to tailor a custom CytoSure array to your specific requirements. Access our Oligome™ database of fully optimised probes to produce an array matching your precise specifications.

Partner with our experienced designers to create the custom solution you are looking for. Email contact@ogt.com for details.

Cytocell an OGT company

FISH probes

SureSeq™

NGS products

CytoSure™

Array products

CytoSure™, SureSeq™ and myProbes™. For Research Use Only; Not for Use in Diagnostic Procedures.
Cytocell: Some products may not be available in the US.

Oxford Gene Technology Inc
Begbroke Science Park, Begbroke Hill, Woodstock Road, Begbroke, Oxfordshire, OX5 1PF, UK
T: +44(0)1865 856800
E: contact@ogt.com
www.ogt.com

For Cytocell FISH probe orders:

Cytocell Ltd
3-4 Technopark, Newmarket Road, Cambridge, CB5 8PB, UK
T: +44(0)1223 294048
E: orders@cytocell.com
www.cytocell.com

Your local distributor